



## UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460

#### MEMORANDUM

SUBJECT:

Review of Phytotoxicity Studies for Fluroxypyr

DP Barcode D239606

FROM:

Michael Davy, Agronomist

Environmental Risk II Branch

Environmental Fate and Effects Branch (7505C)

Thru:

Elizabeth M. Leovey, Chief

Environmental Risk II Branch

Environmental Fate and Effects Branch (7505C)

TO:

Joanne Miller, PM-23

Registration Division (H7506)

The ERB II reviewed the phytotoxicity data submitted by DowElanco in support of fluroxypyr MHE registration. This data package has non-guideline and non-GLP phytotoxicity studies of the fluroxypyr MHE metabolites. These studies were submitted as tier III plant data. However, these studies are useful for tier I plant data only.

Tier I seedling emergence and vegetative vigor data are needed for two species of monocotsrepresenting two families and two species of dicots for methoxypyridine and pyridinol. Tier II vegetative vigor and seedling emergence data are needed for fluroxypyr acid.

The following information is provided:

• CITATION:

Authors:

Wright, J.P., L.B. Rowland

Title: Phytotoxicity of Fluroxypyr MHE and Its Metabolites

Fluroxypyr, Methoxypyridine, and Pyridinol to Non-target

Terrestrial Plants

Study\_Completion\_Date:

Nov. 20, 1995; Amended Aug. 23, 1996

Laboratory:

Global Environmental Chemistry Laboratory DowElanco,

Indianapolis, IN

Sponsor:

DowElanco

Laboratory\_Report.ID: GH-C 3859

MRID No.: 44094902

DP Barcode: D239606

The highest dose tested is 0.5 lb. Ai/A. The reviewer has decided not to review the fluroxypyr MHE because the authors of the study have indicated that 123-1 guideline study is being done for fluroxypyr MHE.

These studies are scientifically sound but do not meet any of the guidelines for phytotoxicity to non-target plants due to the following reasons:

## Bentgrass:

- Testing was not done under GLP
- Height and weight measurements were not taken.

## Lemna gibba

- The study was conducted for 11 days instead of 14 days.
- Testing was not done under GLP
- Dose range was 10X. This makes the tier II plant study invalid.
- Lemna minor was used instead of Lemna gibba.
- Raw data were not provided.
- Light intensity was not reported.

## Seedling Emergence and Vegetative Vigor

- Dose range is 10X instead of 2X or 3X
- Non-GLP
- Insufficient population per replicates used insufficient number of plants. At least 10 seeds per replicate for seedling emergence and five plants per replicate for vegetative vigor is required.
- Insufficient number of species used used three monocots (one family) and four dicots for seedling emergence and two moncots (one family) and four dicots for vegetative vigor. At least four monocots (two families) and six dicots are required.
- Inadequate raw data were supplied.

#### **CONCLUSIONS:**

## Lemna gibha

122-2 tier I study: fluroxypyr MHE and acid, methoxypyridine and pyridinol at maximum rate (0.25 lb. ai/A) do not inhibit *Lemna* sp. more than 50%.

## Seedling Emergence

Methoxypyridine and pyridinol both do not exhibit greater than 25% inhibition on the species tested. Therefore, a tier II seedling emergence study is not needed for the species tested (cotton, radish, soybean, sunflower, corn, and wheat). However, tier I seedling emergence data are still needed for two species of monocots representing two families and two more species of dicots for methoxypyridine and pyridinol. Tier I can be passed over and tier II tested for the above species if the registrant desires.

All of the species tested except radish and corn were inhibited by more than 25% from fluroxypyr acid at application rates up to 0.25 lb. ai/A. Tier II seedling emergence data are outstanding for three species of monocots (not including corn) representing two families and five species of dicots (not including radish) since it appears that the acid degradate may be more phytotoxic than the ester.

## Vegetative Vigor

Methoxypyridine and pyridinol do not exhibit greater than 25% inhibition on the species tested. Therefore, a tier II vegetative vigor study is not needed for the species tested (cotton, radish, soybean, sunflower, corn, and wheat). However, tier I vegetative vigor data is still needed for two other species of monocots representing two families and two more species of dicots. Tier I can be passed over and tier II tested for the above species if the registrant desires.

Fluroxypyr acid does not inhibit corn, wheat, sunflower and radish by more than 25% at rates of application up to 0.5 lb. ai/A. Tier I vegetative vigor data are still needed for fluroxypyr acid on two other species of monocots representing two families and four more species of dicots. Tier I can be passed over and tier II tested for the above species if the registrant desires.

If you have any questions, please do not hesitate to contact Mike Davy at 305-7081.

## DATA EVALUATION RECORD Seedling Emergence EC<sub>25</sub> Test § 122-1(A) AND 123-1(A) (TIER I AND II)

PC Code No.: 128959 1. **CHEMICAL:** Fluroxypyr

2. TEST MATERIAL: Fluroxypyr MHE (99.4%), Fluroxypyr acid (99.6%), Methoxypyridine (99.9%), Pyridinol (99.5%)

3. CITATION

Authors: Wright, J.P., L.B. Rowland

Phytotoxicity of Fluroxypyr MHE and Its Metabolites Title:

Fluroxypyr, Methoxypyridine, and Pyridinol to Non-target

Date: 1/12/98

Terrestrial Plants

Nov. 20, 1995; Amended Aug. 23, 1996 Study Completion Date:

> Laboratory: Global Environmental Chemistry Laboratory DowElanco,

> > Indianapolis, IN

DowElanco Sponsor:

Laboratory Report ID: GH-C 3859

MRID\_No.: 44094902 DP Barcode: D239606

4. REVIEWED BY: Michael Davy, Agronomist, ERBII, EFED

Date: 1/12/93 5. PEER REVIEWED BY: Nicholas Mastrota, Biologist, ERBII, EFED

Nicholas Mastrota

6. STUDY PARAMETERS

Signature:

**Definitive Study Duration:** 11 days for bentgrass, others are 26 days

7. **CONCLUSIONS:** This study is not scientifically sound and does not meet the guidelines for a 123-1(a) seedling emergence tier II study. No Ec, values from this study should be used for risk assessment.

However, this study is scientifically sound but does not meet all of the guidelines for a 122-1 (a) seedling emergence tier I study using methoxypyridine and pyridinol. Methoxypyridine and pyridinol both do not exhibit greater than 25% inhibition some of the species. Therefore, a tier II seedling emergence study is not needed for the species tested (cotton, radish, soybean, sunflower, corn, and wheat). However, tier I seedling

emergence data is still needed for two species of monocots (including bentgrass) representing two families and two more species of dicots for methoxypyridine and pyridinol. Tier I can be passed over and tier II tested for the above species if the registrant desires.

Tier I seedling emergence for fluroxypyr ester and acid has determined that corn and radish may not be tested for tier II seedling emergence since the species were not inhibited more than 25% at rates of application up to 0.25 lb. ai/A. Therefore, tier II seedling emergence data is outstanding for three species of monocots (including bentgrass) representing two families and five species of dicots since it appears that the acid may be more phytotoxic than the ester. Phytotoxicity data is required for fluroxypyr acid, a degradate of fluroxypyr MHE.

## 8. ADEQUACY OF THE STUDY

A. Classification: Invalid for 123-1 (b) - tier II

Supplemental for 122-1 (b) - tier I

#### B. Rationale:

Invalid- 123-1(b) tier II - Too large a dose range (10X) and non GLP study. Supplemental - 122-1(a) tier I - Non-GLP study and insufficient number of species tested and plant population.

C. Repairability: none for 123-1(b) tier II; for tier I, test the above species or go to tier II testing for the species as described in the conclusion section.

## 9. GUIDELINE DEVIATIONS

- 1. Dose range is 10X instead of 2X or 3X
- 2. Non-GLP
- 3. Insufficient population per replicates used five seeds instead of minimum of 10 seeds
- 4. Bentgrass used only a visual symptom parameter no height or weight taken.
- 5. Insufficient number of species used used three monocots (one family) and four dicots, should have four monocots (two families) and six dicots.
- 6. Inadequate raw data was supplied.
- 10. SUBMISSION PURPOSE: section 3 registration

#### 11. MATERIALS AND METHODS

The Reviewer has decided to review the metabolite data and not the chemical being registered, Fluroxypyr MHE since this chemical is also being tested under GLP 123-1 guidelines. Therefore, the materials, methods, and results will be of the metabolites.

## A. Test Organisms

Guideline Criteria	Reported Information
Species 6 dicots in 4 families, including soybean and a rootcrop; 4 monocots in 2 families,	Dicots: cotton, radish, soybean, sunflower
including corn.	Monocots: corn, wheat, bentgrass
Number of seeds per rep: 10	3 ml of seed/media mixture for bentgrass, 5 seeds for cotton, soybean, sunflower, corn; 20 seeds for radish and corn
Source of Seed	unknown

## B. Test System

Guideline Criteria	Reported Information
Solvent	DMSO
Site of test	greenhouse and growth chamber
Planting method / type of pot	for bentgrass: 3 ml of growth media into 12 wells of sterile culture plate. For others: 14 cm round plastic pots with mineral soil mix.
Method of application	bentgrass: dropper. 20 gpa track sprayer for others
Method_of watering: bottom- water	bentgrass: none. Lightly top watered for others

# C. Test Design

Guideline Criteria	Reported Information
Dose range: 2x or 3x	10X
Doses: At least 5	5
Controls: Negative and solvent	negative and solvent
Replicates per dose: At least 3	3
Duration of test 14 days	11 days for bentgrass, others are 26 days after treatment
Were observations made at least weekly?	Yes
Maximum labeled rate	560 mg/ha ( 0.5 lb ai/A)

## 12. REPORTED RESULTS

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	This is not GLP.
Was a NOEC observed for each species?	Yes
Phytotoxic observations	yes
Were initial chemical concentrations measured? (Optional)	No
Were adequate raw data included?	No

EC<sub>25</sub> results of the most sensitive parameter of each species

Species	Fluroxypyr MHE	Fluroxypyr acid	Methoxypyridine	Pyridinol
Com	>560	>560	>560	>560
Wheat	170.4 Plant height	89.2 Fresh weight	>560	>560
Sunflower	111.0 Fresh weight	27.2 Fresh weight	>560	>560
Cotton	97.4 Fresh weight	28.2 Fresh weight	>560	>560
Soybean	149.8 Fresh weight	80.6 Fresh weight	>560	>560
Radish	>560	331.0 Fresh weight	>560	>560
Bentgrass <sup>2</sup>	7,100 ppb	3,800 ppb	4,100 ppb	41,500 ppb

Determination of the most sensitive species is based on EC2 values in gm ai/ha unless otherwise noted.

## 13. Verification of Statistical Results

## EC25 results of the most sensitive parameter of each species

Species	Fluroxypyr MHE	Fluroxypyr acid	Methoxypyridine	Pyridinol
Corn	461.0 (0.41126)	200.0 (0.17842)	> 560 (0.50000)	> 560 (0.50000)
	Fresh weight	Fresh weight	All parameters	All parameters
Wheat	170.4 (0.15201)	89.2 (0.07958)	> 560 (0.50000)	>560 (0.50000)
	Plant height	Fresh weight	All parameters	All parameters
Sunflower	148.9 (0.13283)	40.0 (0.03568)	>560 (0.50000)	> 560 (0.50000)
	Fresh weight	Height	All parameters	All parameters
Cotton	97.4 (0.08690)	28.2 (0.02516)	>560 (0.50000)	> 560 (0.50000)
	Fresh weight	Fresh weight	All parameters	All parameters
Soybean	149.8 (0.13363)	80.6 (0.07190)	> 560 (0.50000)	>560 (0.50000)
	Fresh weight	Fresh weight	All parameters	All parameters
Radish	>560 (0.50000)	331.0 (0.29529)	>560 (0.50000)	>560 (0.50000)
	All parameters	Fresh weight	All parameters	All parameters
Bentgrass <sup>2</sup>	7,100 ppb	3,800 ppb	4,100 ppb	41,500 ppb

Determination of the most sensitive species is based on EC<sub>23</sub> values in gm ai/ha with 1b ai/A in parenthesis unless otherwise noted. Only visual injury was observed. No information was provided that would indicate now ppm or ppb would be converted to 1b ai/A.

Only visual injury was observed. No information was provided that would indicate how ppm or ppb would be converted to lb ai/A.

## 14. REVIEWER'S COMMENTS

The study cannot be considered a valid study for a tier II seedling emergence 123-1(a) guideline. This study appears to be range finding study to determine levels of phytotoxicity prior to a dose response study. There is a lack of raw data that can be used for statistical analysis of continuous data, therefore a regression analysis was used. The 10X dose range does present some difficulty in the confidence of the regression analysis.

Although this study does not fulfill the guidelines nor is GLP, it does provide some useful information concerning phytotoxicity of the various degradates of fluroxypyr MHE.

It appears that the acid degradate is more toxic to plants than the ester parent. It also appears that the methoxypyridine and pyridinol may exhibit little if any phytotoxicity. Since there is an insufficient number of species and replicate population there is an uncertainty in what the results may mean. However, the visual symptoms and apparent lack of inhibition suggests that there are no phytotoxic mechanisms from methoxypyridine and pyridinol. Therefore, a tier II seedling emergence will not be needed for the species tested (cotton, radish, soybean, sunflower, corn, and wheat). However, two monocot species representing two families and two dicots still need to be tested under tier I seedling emergence.

The bentgrass study does not provide any useful information since the study was done in a fashion of using ppb instead of lb. ai/A or gm ai/ha. It does appear that the methoxypyridine may exhibit some phytotoxicity toward bentgrass that are almost as sensitive as the acid. It appears that pyrindinol does not exhibit any phytotoxcity toward bentgrass.

# DATA EVALUATION RECORD Vegetative Vigor EC<sub>25</sub> Test § 122-1(B) AND 123-1(B) (TIER I AND II)

1. CHEMICAL: Fluroxypyr

PC\_Code\_No\_:128959

2. TEST MATERIAL: Fluroxypyr MHE(99.4%), Fluroxypyr acid (99.6%), Methoxypyridine (99.9%), Pyridinol (99.5%)

3. CITATION

Authors: Wright, J.P., L.B. Rowland

Title: Phytotoxicity of Fluroxypyr MHE and Its Metabolites

Fluroxypyr, Methoxypyridine, and Pyridinol to Non-target

Terrestrial Plants

Study Completion Date: Nov. 20, 1995; Amended Aug. 23, 1996

Laboratory: Global Environmental Chemistry Laboratory DowElanco,

Indianapolis, IN

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4. REVIEWED BY: Michael Davy, Agronomist, ERBII, EFED

Signature: MMaet Jam

Date: 1/12/93 D

Date: 1/12/98

5. PEER REVIEWED BY: Nicholas Mastrota, Biologist, ERBII, EFED

Signature: Nicholas Mastrota

6. STUDY PARAMETERS

**Definitive Study Duration: 26 days** 

7. CONCLUSIONS: This study is not scientifically sound and does not meet the guidelines for a 123-1(b) vegetative vigor tier II study. No Ec<sub>25</sub> values from this study should be used for risk assessment.

However, this study is scientifically sound but does not meet all of the guidelines for a 122-1 (b) vegetative vigor tier I study using methoxypyridine and pyridinol. Methoxypyridine and pyridinol both do not exhibit greater than 25% inhibition. Therefore, a tier II vegetative vigor study is not needed for the species tested (four dicots and two grass monocots). However, tier I vegetative vigor data is still needed for two species of monocots (including bentgrass) representing two families and two

more species of dicots. Therefore, the study is supplemental as a tier I vegetative vigor study. It is determined that additional tier II vegetative vigor testing is not needed for the species tested (cotton, radish, soybean, sunflower, corn, and wheat). However, tier I vegetative vigor data is still needed for two species of monocots (including bentgrass) representing two families and two more species of dicots. Tier I can be passed over and tier II tested for the above species if the registrant desires.

Tier I vegetative vigor for fluroxypyr acid has determined that corn, wheat sunflower and radish may not be tested for tier II vegetative vigor since the species were not inhibited more than 25% at rates of application upto 0.5 lb ai/A. However, tier I vegetative vigor data is still needed for fluroxypyr acid on two species of monocots (including bentgrass) representing two families and four more species of dicots. Tier I can be passed over and tier II tested for the above species if the registrant desires.

## 8. ADEQUACY OF THE STUDY

**A.** Classification: Invalid for 123-1 (b) - tier II

Supplemental for 122-1 (b) - tier I

#### B. Rationale:

Invalid- 123-1(b) tier II - Too large a dose range (10X) and non GLP study. Supplemental - 122-1(b) tier I - Non-GLP study and insufficient number of species tested.

C. Repairability: none for 123-1(b) tier II; for tier I, test the above species or go to tier II testing for the species as desribed in the conclusion section.

## 9. GUIDELINE DEVIATIONS

- 1. Dose range is 10X instead of 2X or 3X
- 2. Non-GLP
- 3. Insufficient number of species used used two moncots (one family) and four dicots, should have four monocots (two families) and six dicots.
- 4. Too few seeds per reps.
- 5. Inadequate raw data were supplied.

## 10. SUBMISSION PURPOSE: section 3 registration

## 11. MATERIALS AND METHODS

The Reviewer has decided to review the metabolite data and not the chemical being registered, Fluroxypyr MHE since this chemical is also being tested under GLP 123-1 guidelines. Therefore, the materials, methods, and results will be of the metabolites.

## A. Test Organisms

Guideline Criteria	Reported Information
Species: Six dicots in four families, including soybean and a rootcrop; four monocots in two families, including com.	Dicals: cotton, radish, soybean, sunflower Manacals: corn, wheat
Number of seeds per rep: 10	five plants for cotton, soybean, sunflower, corn; 20 plants for radish and wheat
Source of Seed	unknown

## B. Test System

Guideline Criteria Reported Information			
Solveat	DMSO		
Site of test	greenhouse		
Planting method / type of pot	14 cm round plastic pots with mineral soil mix.		
Method of application	20 gps track sprayer for others		
Method of watering: bottom- water	- Rottom-waterèd		

## C. Test Design

Guideline Criteria Reported Information			
Dose range: 2x or 3x	10X		
Doses: At least five	five		
Controls: Negative and solvent	negative and solvent		
Replicates per dose: At least three	three		
Duration of test: 14 days	26 days after treatment		
Were observations made at least weekly?	Yes		
Maximum labeled rate	max. dose is 560 mg/ha (0.5 lb ai/A) and max. rate of application is 0.25 lb ai/A.		

## 12. REPORTED RESULTS

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	This is not GLP.
Was a NOEC observed for each species?	Yes
Phytotoxic observations	yes
Were initial chemical concentrations measured? (Optional)	No
Were adequate raw data included?	No

## EC<sub>25</sub> results of the most sensitive parameter<sup>1</sup> of each species

Species	Fluroxypyr MHE	Fluroxypyr acid	Methoxypyridine	Pyridinol
Com	>560	> 560	>560	>560
Wheat	> 560	> 560	> 560	> 560
Sunflower	> 560	> 560	> 560	>560
Cotton	ND	ND	> 560	> 560
Soybean	ND	ND	>560	> 560
Radish	> 560	> 560	> 560	> 560

Determination of the most sensitive species is based on EC23 values in gm ai/ha unless otherwise noted.

Only visual injury was observed. No information was provided that would indicate how ppm or ppb would be converted to lb ai/A.

Not determined or insufficient dose response to calculate these values.

## 13. Verification of Statistical Results

EC<sub>25</sub> results of the most sensitive parameter<sup>1</sup> of each species

Species	Fluroxypyr MHE	Fluroxypyr acid	Methoxypyridine	Pyridinol
Сот	> 560 (0.50000) All parameters	>560 (0.50000) All parameters	> 560 (0.50000) All parameters	> 560 (0.50000) All parameters
Wheat	> 560 (0.50000) All parameters	>560 (0.50000) All parameters	> 560 (0.50000) All parameters	>560 (0.50000) All parameters
Sunflower	ND,	ND,	>560 (0.50000) All parameters	>560 (0.50000) All parameters
Cotton	8.08 (0.00721) Fresh weight	ND,	>560 (0.50000) All parameters	> 560 (0.50000) All parameters
Soybean	0.47 (0.00042) Height	0.75 (0.00067) Height	> 560 (0.50000) All parameters	> 560 (0.50000) All parameters
Radish	>560 (0.50000)	>560 (0.50000)	> 560 (0.50000)	> 560 (0.50000)

Determination of the most sensitive species is based on EC<sub>22</sub> values in gm ai/ha with lb ai/A in parenthesis unless otherwise noted. Only visual injury was observed. No information was provided that would indicate how ppm or ppb would be converted (gm ai/ha x 0.0008921 lb ai/A) to lb ai/A.

## 14. REVIEWER'S COMMENTS

The study cannot be considered a valid study for a vegetative vigor 123-1 guideline (tier II). This study appears to be range finding study to determine levels of phytotoxicity prior to a dose response study. There is a lack of raw data for statistical analysis of continuous data. Therefore, a regression analysis was used. The 10X dose range presents much difficulty in the confidence of the regression analysis. The  $EC_{25}$  values from this study cannot be used for risk assessment purposes.

Although this study does not fulfill the guidelines nor is GLP, it does provide some useful information concerning phytotoxicity of the various degradates of fluroxypyr MHE. It appears that the methoxypyridine and pyridinol may exhibit little if any phytotoxicity. Since at the maximum dose rate (which is twice the maximum application rate), methoxypyridine and pyridinol both do not exhibit greater than 25% inhibition. Therefore, as a tier I vegetative vigor study the study is supplemental but can be used to determine that additional tier II vegetative vigor testing is not needed for the species tested (four dicots and two grass monocots). However, tier I vegetative vigor data is still needed for more two species of monocots (including bentgrass) representing two families and two more species of dicots.

The bentgrass study does not provide any useful information since the study was done in a fashion of using ppb instead of lb ai/A or gm ai/ha. It does appear that the

Not Determined due to no statistical confidence of the values or slope, or 50% inhibition occurred at lowest concentration.

methoxypyridine may exhibit some phytotoxicity that is almost as sensitive as the acid. It appears that pyrindinol does not exhibit any phytotoxcity toward bentgrass. The reviewer believes that tier I study using bentgrass is useful provided that the other parameters besides visual injury observation would be used, i.e., fresh weight or height.

The fluroxypyr acid appears to be similar to fluroxypyr MHE in toxicity. However, there are uncertainty in this due to the wide range of dose, non-GLP, and lack of species tested.

## DATA EVALUATION RECORD EC50 TEST WITH LEMNA GIBBA GUIDELINE 122-2 OR 123-2 (TIER I OR II)

1. **CHEMICAL:** Fluroxypyr

PC Code No.: 128959

2. TEST MATERIAL: Fluroxypyr MHE(99.4%), Fluroxypyr acid (99.6%), Methoxypyridine (99.9%), Pyridinol (99.5%)

3. CITATION

Wright, J.P., L.B. Rowland Authors:

Phytotoxicity of Fluroxypyr MHE and Its Metabolites Title:

Fluroxypyr, Methoxypyridine, and Pyridinol to Non-target

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Study Completion Date: Nov. 20, 1995; Amended Aug. 23, 1996

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> > Indianapolis, IN

Sponsor: DowElanco

Laboratory Report ID: GH-C 3859

> MRID\_No\_: 44094902 DP Barcode: D239606

4. REVIEWED BY: Michael Davy, Agronomist, ERBII, EFED

5. PEER REVIEWED BY: Nicholas Mastrota, Biologist, ERBII, EFED

Signature: Nicholas Miastcota

Date: 1/12/98Date: 1/12/98

STUDY PARAMETERS

Definitive Test Duration: 11 days Type of Concentrations: Nominal

- 7. **CONCLUSIONS:** 122-2 tier I study: fluoxypyr MHE and acid, methypyridine and pyridinol at maximum rate (0.25 lb ai/A) do not inhibit Lemna sp. more than 50%.
- ADEOUACY OF THE STUDY
  - Classification: 123-2 tier II study is Invalid. 122-1 tier I study is supplemental.
  - B. Rationale: For the tier II study: non-GLP and too large a range of dose response. For the tier I study: study is non-GLP, wrong species is used, study was conducted for 11 days instead of 14 days.

## C. Repairability: None

## 9. GUIDELINE DEVIATIONS

- 1. The study was conducted for 11 days instead of 14 days.
- 2. This is not a GLP study
- 3. Dose range was 10X. This makes the tier II plant study invalid.
- 4. Lemna minor was used instead of Lemna gibba.
- 5. Light intensity was not reported.
- 6. Raw data was not provided.

## 10. **SUBMISSION PURPOSE:** registration 3

## 11. MATERIALS AND METHODS

## A. Test Organisms

Guideline Criteria	Reported Information
<u>Species</u> : Lemna gibba	Lemna minor
Number of Plants/Fronds 5 plants, 3 fronds per plant.	12 plants with 3 fronds each per replicate
Nutrients Standard formula, e.g. 20XAAP	Standard formula

## B. Test System

Guideline Criteria Reported Information				
Solvent	DMSO			
Temperature : 25°C	27.°C			
Light Intensity: 5.0 Lux (±15%)	Lux was not given			
Photoperiod : Continuous	Continuous			
pH : Approximately 5.0	6.5			
Test System: Static or renewal	static			

## C. Test Design

Guideline Criteria	Reported Information
<u>Dose range:</u> 2X or 3X progression	10X
Doses: at least 5	6

Guideline Criteria	Reported Information
Controls negative and/or solvent	both
Replicates per dose 3 or more	3
Duration of test: 14 days	11 days
Daily observations were made?	Yes
Method of Observations	visual
Maximum Labeled Rate	0.25 lb ai/acre

## 12. REPORTED RESULTS

Guideline Criteria Reported Information				
Initial and 14 day frond count?	No, (fronds were counted on day 11 instead of day 14)			
Control frond count at 14 day	Not reported			
Initial chemical concentrations measured? (Optional)	No			
Raw data included?	No			

Dose Response

. His married	fluorxypyr acid		Пиогхуруг МНЕ		pyrindinol		methoxypyridine	
Dose (mg ai/L)	Number of fronds	% Inhibition	Number of fronds	% Inhibition	Number of fronds	% Inhibition	Number of fronds	% Inhibition
Control	79	na -	na	na na	na	na	na	na
Solvent Control	· 71	na	na	na na	na	na	na	na
0.001	NR¹	0	NR¹	0	NR'	0	NR'	0
0.01	NR <sup>1</sup>	0	NR1	0	NR¹	0	NR¹	0
0.1	NR <sup>1</sup>	0	NR1	0	NR¹	0	NR1	0
1.0	85	0	41	45	44	41	43	43
10	39	48	29	61	26	65		65
100	3	96	34	55	1	99	1	99

Other Significant Results: Fluoxypyr acid and MHE started showing visual injury (12%) at 1 ppm, pyrindinol at 1 ppm (5% injury) and methoxypyridine at 0.1 ppm (5% injury). Methoxypyridine appears to have a probable outlier at 10 ppm dose.

## Statistical Results

The below EC50 results are for visual injury:

fluorxypyr acid  $EC_{50} = 7.7$  ppm fluorxypyr MHE  $EC_{50} = 103.4$  ppm Methoxypyridine  $EC_{50} = 8.0$  ppm Pyridinol  $EC_{50} = 15.5$  ppm

The author did not do  $EC_{50}$  calculations for number of fronds or biomass.

## 13. Verification of Statistical Results and REVIEWER'S COMMENTS:

This study is scientifically valid but does not meet the guidelines for 122-2 tier I aquatic plant study using Lemna sp. This study is invalid for use as guideline 123-2 tier II aquatic plant study.

Since the dose range (10X) is too wide a range to have good confidence on the dose response curve, the reviewer did not attempt to calculate the  $EC_{50}$  values.

It appears that the 50% inhibition level (about 1 ppm) for fluoxypyr MHE, methoxypyridine and pyridinol would be under the EEC associated with the maximum application rate of 0.25 lb ai/A. (0.25 lb ai/A x 274 ppb/lb ai/A = 181 ppb). Fluroxypyr MHE seems to be less sensitive than the other compounds to Lemna sp. Actually, the reason that the MHE appears to be less toxic is that it is very insoluble in water. Nominal concentrations were as high as 100 ppm, but the solubility is only 0.1 ppm. Therefore, only a very small percent of the ai added to the test vessels would have gone into solution. This is why the percent response did not change much as the nominal concentrations increased. All that can be concluded for fluroxypyr MHE is that the EC50 is greater than the solubility limit.

<sup>1</sup> Not reported. The author has indicated that there was no inhibition for any of the compounds below 1 ppm.

It appears that all of the compounds would not exceed the maximum application rate with an inhibition of 50%. Therefore, tier I study for fluroxypyr MHE and it's metabolites is satisfied and tier II study is not needed using the *Lemna* sp.

The confidence of the results of this study as a tier I study is not high because this study was not done using GLP. This study apparently was a screening study for preparation for a tier II plant study.

SOIL APPLICA

1. 625

DAVY FLUROXYPYR ACID CORN WT

*****	****	******	*****	*******
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL
	EXPOSED	DEAD	DEAD	PROB. (PERCENT)
560.	100	47	47	0
280	100	29	29	0
140	100	18	18	0
70	100	18	18	0
3.5	100	0	0	0

BECAUSE THE NUMBER OF ORGANISMS USED WAS SO LARGE, THE 95 PERCENT CONFIDENCE INTERVALS CALCULATED FROM THE BINOMIAL PROBABILITY ARE UNRELIABLE. USE THE INTERVALS CALCULATED BY THE OTHER TESTS.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 0

THE MOVING AVERAGE METHOD CANNOT BE USED WITH THIS DATA SET BECAUSE NO SPAN WHICH PRODUCES MOVING AVERAGE ANGLES THAT BRACKET 45 DEGREES ALSO USES TWO PERCENT DEAD BETWEEN 0 AND 100 PERCENT.

RESULTS CALCULATED USING THE PROBIT METHOD ITERATIONS G H

GOODNESS OF FIT PROBABILITY

4 .684148 4.150108

5.989135E-03

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 1.341092

95 PERCENT CONFIDENCE LIMITS = .2318313 AND 2.450353

LC50 = 637.4688

95 PERCENT CONFIDENCE LIMITS = 285.0717 AND 235090.3

LC10 = 72.02269

95 PERCENT CONFIDENCE LIMITS = .4353495 AND 155.2172

DAVY FLUROXYPYR ESTER CORN WT

****	*********	*******	******	*******
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL
	EXPOSED	DEAD	DEAD	PROB. (PERCENT)
560	100	32	32	0
280	100	12	12	0
140	100	0	0	0
70	100	0.	0	0
35	100	0	0	0

THE BINOMIAL TEST SHOWS THAT 560 AND +INFINITY CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

THE MOVING AVERAGE METHOD CANNOT BE USED WITH THIS DATA SET BECAUSE NO SPAN WHICH PRODUCES MOVING AVERAGE ANGLES THAT BRACKET 45 DEGREES ALSO USES TWO PERCENT DEAD BETWEEN 0 AND 100 PERCENT.

E(25:461.

E ( = 1 - 40.0

RESULTS CALCULATED USING THE PROBIT METHOD ITERATIONS G GOODING OF FIT PROBABILITY

9.617741E-02

1

4518588

SLOPE = 3.132488 95 PERCENT CONFIDENCE LINGTS = 2.161026 AND 4.10395

LC50 = 757.8403

95 PERCENT CONFIDENCE LIMITS = 620.8020 AND 1061.047

297.9541

95 PERCENT CONFIDENCE LIMITS = 241.0279 AND 346.3211

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

DAVY FLUROXYPYR ACID SUNFLOER HT

*****	*******	*****		***************
CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL
560	100	86	86	PROB. (PERCENT)
280	100	64	64	0
140	100	50	50	0
70 2.5	100	43	43	0
35	100	21	21	0

THE BINOMIAL TEST SHOWS THAT 140 AND 140 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 140

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

G LC50 95 PERCENT CONFIDENCE LIMITS 4 3.870413E-02 124.8129 103.204

149.5569

RESULTS CALCULATED USING THE PROBIT METHOD ITERATIONS "

GOODNESS OF FIT PROBABILITY

4.273469E-02

.2129521

SLOPE = . 1.394177

95 PERCENT CONFIDENCE LIMITS = 1.105968 AND 1.682387

LC50 = 121.8159

95 PERCENT CONFIDENCE LIMITS = 99.38064 AND 147.9125

LC10 = 14.95453

95 PERCENT CONFIDENCE LIMITS = 8.096956 AND 22.68768

# DAVY FLUROXYPYR ESTER SUNFLOWER HT

* * * * * * *	• * * * * * * * * * * * * * *	**********	******	************	سينسديد.
CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCE	,
560	100	50	50	O PERCE	
280	100	50	50		
140	100	. 29	29	· 😈	
70	100	21	21	0	
35	100	0	<u></u>	0	

THE BINOMIAL TEST SHOWS THAT 550 AND 280 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 395.9798

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

 SPAN
 G
 LC50
 95 PERCENT CONFIDENCE LIMITS

 2
 .4155988
 395.9798
 268.6642
 955.4648

RESULTS CALCULATED USING THE PROBIT METHOD ITERATIONS G H

GOODNESS OF FIT PROBABILITY

0

.7274409 5.679876

A PROBABILITY OF 0 MEANS THAT IT IS LESS THAN 0.001.

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 1.424625

95 PERCENT CONFIDENCE LIMITS = .2095603 AND 2.63969

LC50 = 386.4365

95 PERCENT CONFIDENCE LIMITS = 177.7151 AND 49245.25

LC10 = 49.61526

95 PERCENT CONFIDENCE LIMITS = 2.147287E-02 AND 117.1578

DAVY FLUROXYPYR ACID SUNFLOWER WT

			****	* * * * * * * * * * * * * * * * * * *	*****
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL	,
	EXPOSED	DEAD	DEAD	PROB. (PERCENT)	1111
560	100	100	100	0	
280	100	· 85	85	0	· /

= 129.8

ECZ.

140	100	54	54	0
70	100	31	31	0
35	100	23	23	0

THE BINOMIAL TEST SHOWS THAT 70 AND 140 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 124.3942

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

 SPAN
 G
 LC50
 95 PERCENT CONFIDENCE LIMITS

 4
 1.845582E-02
 102.5911
 89.30089

116.4893

RESULTS CALCULATED USING THE PROBIT METHOD ITERATIONS G H

EC25 = 50.0

DDNESS OF FIT PROBABILITY

5 .3056977 4.809713

2.375007E-03

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 2.277929 ... 95 PERCENT CONFIDENCE LIMITS = 1.018464 AND 3.537395

LC50 = 99.05019 95 PERCENT CONFIDENCE LIMITS = 52.10558 AND 164.3521

LC10 = 27.43667 95 PERCENT CONFIDENCE LIMITS = 4.068872 AND 52.14198

DAVY FLUROXYPYR ESTER SUNFLOWER WT

		*********	* * * * * * * * * * * * * * * * * * *		
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL	
	EXPOSED	DEAD	DEAD	PROB. (PERCENT)	
560	100.	77	77	0	
280	100	62	62	0	
140	100	31	31	0	
70	100	Э	0	0	
35	100	0	0	0	

THE BINOMIAL TEST SHOWS THAT 140 AND 280 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 214.6458

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN G LC50 95 PERCENT CONFIDENCE LIMITS

242.8208 218.3732

272.0861

3

RESULTS CALCULATED USING THE PROBIT METHOD ITERATIONS G

GOODNESS OF FIT PROBABILITY

.3410668 5.325073

1.147628E-03

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 2.91321

95 PERCENT CONFIDENCE LIMITS = 1.211868 AND 4.614551

LC50 = 253.9342

95 PERCENT CONFIDENCE LIMITS = 160.0839 AND 473.1942

LC10 = 93.06273

95 PERCENT CONFIDENCE LIMITS = 23.99428 AND 150.0012

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

DAVY FLUROXYPYR ACID COTTON HT

^^^^		*********	* * * * * * * * * * * * * * * * * * * *		
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL	
	EXPOSED	DEAD	DEAD	PROB. (PERCENT)	
560	100 .	.84	84	0	
280	100	67	67	0	
140	100	67 <sup></sup>	67	0	
70	100	51	51	0	
35	100	51	51	0	

THE BINOMIAL TEST SHOWS THAT 0 AND 35 CAN RE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

EC2= 148.4

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 70

THE MOVING AVERAGE METHOD CANNOT BE USED WITH THIS DATA SET BECAUSE NO SPAN WHICH PRODUCES MOVING AVERAGE ANGLES THAT BRACKET 45 DEGREES ALSO USES TWO PERCENT DEAD BETWEEN 0 AND 100 PERCENT.

RESULTS CALCULATED USING THE PROBIT METHOD ITERATIONS G

GOODNESS OF FIT PROBABILITY

.1309839 1

.1962962

SLOPE = .7566037

95 PERCENT CONFIDENCE LIMITS = .482776 AND 1.030432

LC50 = 44.3166

95 PERCENT CONFIDENCE LIMITS = 21.12628 AND 67.44109

95 PERCENT CONFIDENCE LIMITS = 5.482506E-02 AND 3.561687

DAVY	FLUROXYPYR	ESTER	COTTON	${ m HT}$

*****	******************			*******
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL
	EXPOSED	DEAD	DEAD	PROB. (PERCENT)
560	100	67	67	0
280	100	51	51	0
140	100	43	43	0 .
70	100	35	35	0
3.5	100	18	1.8	0

THE BINOMIAL TEST SHOWS THAT 140 AND 280 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 256.8222

EC2- 41.9

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

95 PERCENT CONFIDENCE LIMITS SPAN G LC50 220.0709 .1837875 155.3767 326.9033 3

RESULTS CALCULATED USING THE PROBIT METHOD ITERATIONS G

GOODNESS OF FIT PROBABILITY

7.286925E-02 1 .5973874

SLOPE ·= 1.021491

95 PERCENT CONFIDENCE LIMITS = .7457463 AND 1.297235

LC50 = 219.3803

95 PERCENT CONFIDENCE LIMITS = 169.1272 AND 302.528

LC10 =12.529

95 PERCENT CONFIDENCE LIMITS = .4.784321 AND 22.24137

DAVY FLUROXYPYR ACID COTTON WT

*****	*******	* * * * * * * * * * * * * *	*****	********		
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL		
	EXPOSED	DEAD	DEAD	PROB. (PERCENT)		
560	100	89	89	0		
280	100	67	67	0		
140	100	67	67	0		
70	100	33	33	0		
35	100	22	22	0		

THE BINOMIAL TEST SHOWS THAT 70 AND 140 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 98.99491

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN G LC50 95 PERCENT CONFIDENCE LIMITS

4 3.536337E-02 111.0836 91.88477

132.0351

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS G H

= 41.3 EC25

GOODNESS OF FIT PROBABILITY

3 .2576404 2.784106

3.926492E-02

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 1.602422

95 PERCENT CONFIDENCE LIMITS = .78906 AND 2.415784

LC50 = 109.0636

95 PERCENT CONFIDENCE LIMITS = 59.04931 AND 178.7079

LC10 = 17.58447

95 PERCENT CONFIDENCE LIMITS = 2.023521 AND 38.1972

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DAVY FLUROXYPYR ESTER COTTON WT

280 100 56 56 0 100 140 33 33 0 70 100 11 11 0 35 100

THE BINOMIAL TEST SHOWS THAT 140 AND 280 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 234.2243

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN G LC50 95 PERCENT CONFIDENCE LIMITS

3 5.086846E-02 261.7655 219.4511

321.7259

RESULTS CALCULATED USING THE PROBIT METHOD ITERATIONS G H
GOODNESS OF FIT PROBABILITY

11/

3.465831E-02

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

£025 - 130.2

SLOPE = 2.073583

95 PERCENT CONFIDENCE LIMITS = 1.095144 AND 3.052022

LC50 = 275.612

95 PERCENT CONFIDENCE LIMITS = 184.8889 AND 504.1882

LC10 = 67.2716

95 PERCENT CONFIDENCE LIMITS = 22.74204 AND 108.8658

#### DAVY FLUROXYPYR ACID SOYBEAN HT \*

NUMBER PERCENT CONC. NUMBER BINOMIAL DEAD EXPOSED DEAD PROB. (PERCENT) 67 560 100 67 Ω 280 100 43. 43 0 27 140 100 27 70 100 18 18 35 100

THE BINOMIAL TEST SHOWS THAT 280 AND 560 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 341.9285

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN G LC50 . 95 PERCENT CONFIDENCE LIMITS

.1147403 332.9144 271.5883 426.8164

RESULTS CALCULATED USING THE PROBIT METHOD ITERATIONS G

GOODNESS OF FIT PROBABILITY

3.666595E-02

.1996227

SLOPE 1.726019

95 PERCENT CONFIDENCE LIMITS = 1.395515 AND 2.056524

LC50 = 319.22

95 PERCENT CONFIDENCE LIMITS = 266.0969 AND 398.9089

LC10 = 58.65335

95 PERCENT CONFIDENCE LIMITS = 42.1069 AND 74.80916

#### DAVY FLUROXYPYR ESTER SOYBEAN HT

****	********	******	*******		
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL	
	EXPOSED	DEAD	DEAD	PROB. (PERCENT)	
560	100	43	43	0	
280	100	27	27	0	
140	100	10	10	0	
70	100	10	10 .	0	
35	100	2	2	0	

THE BINOMIAL TEST SHOWS THAT 560 AND +INFINITY CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 560

THE MOVING AVERAGE METHOD CANNOT BE USED WITH THIS DATA SET BECAUSE NO SPAN WHICH PRODUCES MOVING AVERAGE ANGLES THAT BRACKET 45 DEGREES ALSO USES TWO PERCENT DEAD BETWEEN 0 AND 100 PERCENT.

261.1

RESULTS CALCULATED USING THE PROBIT METHOD ITERATIONS G H

GOODNESS OF FIT PROBABILITY

3

6.484695E-02

7

.3189736

SLOPE = 1.44307

95 PERCENT CONFIDENCE LIMITS = 1.075591 AND 1.810548

LC50 = 768.5995

95 PERCENT CONFIDENCE LIMITS = 554.3388 AND 1271.467

LC10 = 101.3053

95 PERCENT CONFIDENCE LIMITS = 70.73917 AND 130.6862

#### DAVY FLUROXYPYR ACID SOYBEAN WT

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CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL
	EXPOSED	DEAD .	DEAD	PROB. (PERCENT)
560	100	73	73	0
280	100	87	87	0
140	100	33	33	0
70	100	33	· 33	0
35	100	7	7	0

THE BINOMIAL TEST SHOWS THAT 140 AND 280 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 171.7101

20

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

G LC50 95 PERCENT CONFIDENCE LIMITS

3.434281E-02 4

149.2322 125.7654

177.8838

PESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS G

GOODNESS OF FIT PROBABILITY

.982835 12.57805

0

A PROBABILITY OF 0 MEANS THAT IT IS LESS THAN 0.001.

EC25 69.0

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE

1.807582

95 PERCENT CONFIDENCE LIMITS = 1.558054E-02

AND 3.599583

LC50 = 163.0198

95 PERCENT CONFIDENCE LIMITS = 5.76855 AND 2.180467E+08

LC10 = 32.33285

95 PERCENT CONFIDENCE LIMITS = 5.877472E-39 AND 89.94549

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DAVY FLUROXYPYR ESTER SOYBEAN WT

^ ^ ^ ^ ^ ^ ^ ^				
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL
	EXPOSED	DEAD	DEAD	PROB. (PERCENT)
560	100	73	73	0
280	100	33	33	0 .
140	100	47	47	0 .
70	100	7	7	0
35	100	20	20	0

THE BINOMIAL TEST SHOWS THAT 280 AND 560 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 374.7879

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN

G

LC50 95 PERCENT CONFIDENCE LIMITS

3 3.434281E-02 271.0279

233.9967

321.0097

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS

GOODNESS OF FIT PROBABILITY

1:85271 13.12927

0

A PROBABILITY OF 0 MEANS THAT IT IS LESS THAN 0:001.

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE 1.262477

95 PERCENT CONFIDENCE LIMITS =-.4559343 AND 2.980888

LC50 = 294.0551

95 PERCENT CONFIDENCE LIMITS = 0 AND +INFINITY

LC10 =29.0048

95 PERCENT CONFIDENCE LIMITS = 0 AND 113.4353

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#### DAVY FLUROXYPYR ACID RADISH WT

********			*****	*****		
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL		
	. EXPOSED	DEAD	DEAD	PROB. (PERCENT)		
560	100	73	73	0		
280	100	14	14	0		
140	100	0	0	0		
70	100	0	0 .	0		
35	100	9	9	0		

THE BINOMIAL TEST SHOWS THAT 280 AND 560 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 432.3077

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

95 PERCENT CONFIDENCE LIMITS G LC50 SPAN Jour set No ecu pessisi

432.3077 400.789 1 .0476546 470.4194

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS G

GOODNESS OF FIT PROBABILITY

0

5.536991 47.39062 б

A PROBABILITY OF 0 MEANS THAT IT IS LESS THAN 0.001.

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

2.10449

95 PERCENT CONFIDENCE LIMITS = 0 AND +INFINITY

LC10 = 128.0794

95 PERCENT CONFIDENCE LIMITS = 0 AND +INFINITY

95 PERCENT CONFIDENCE LIMITS = -2.847546 AND 7.056526 LC50 =513.9855

Por set

DAVY FLUROXYPYR ACID WHEAT WT

		* * * * * * * * * * * * * * * * * * *	* * * * * * * * * * * * * * * * * * * *		
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL	
	EXPOSED	DEAD.	DEAD	PROB. (PERCENT)	
560	100	58	58	0	
280	100	46	46	0	
140	100	35	35	0	
70	100	24	24	0	
35	100	0	0	0	

THE BINOMIAL TEST SHOWS THAT 280 AND 560 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 352.6053

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN G LC50 95 PERCENT CONFIDENCE LIMITS

114.1

ECzi

2 .3602092 351.1796 242.4521 656.4488

RESULTS CALCULATED USING THE PROBIT METHOD
ITERATIONS G H
GOODNESS OF FIT PROBABILITY

5 .610739 5.201856

1.365781E-03

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 1.469774

95 PERCENT CONFIDENCE LIMITS = .3211486 AND 2.618399

LC50 = 329.5386

95 PERCENT CONFIDENCE LIMITS = 161.0479 AND 4875.132

LC10 = 45.06378

95 PERCENT CONFIDENCE LIMITS = .2772626 AND 102.9119

DAVY FLUROXYPYR ESTER WHEAT WT

*******		***********		*******
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL
	EXPOSED	DEAD.	DEAD	PROB. (PERCENT)
560	100 .	35.	35	0
280	100	24	24	. 0
140	100	24 '	24	0
70	100	13	13	0
35	100	3	3	0

THE BINOMIAL TEST SHOWS THAT 560 AND +INFINITY CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 560

THE MOVING AVERAGE METHOD CANNOT BE USED WITH THIS DATA SET BECAUSE NO SPAN WHICH PRODUCES MOVING AVERAGE ANGLES THAT BRACKET 45 DEGREES ALSO USES TWO PERCENT DEAD BETWEEN 0 AND 100 PERCENT.

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS G

Η

EC25 = 250.6

GOODNESS OF FIT PROBABILITY

4

.1073404 1

.1385564

SLOPE = .9853856

95 PERCENT CONFIDENCE LIMITS = .6625452

AND 1.308226

LC50 = 1213.672

95 PERCENT CONFIDENCE LIMITS = 709.097 AND 3270.814

LC10 = 62.41168

95 PERCENT CONFIDENCE LIMITS = 32.8707 AND 91.39488

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

05-0			
SLOPE = 199.9886	1.341092 LC50 =	637.4688 LC25 =	
SLOPE = 461.0361	: 3.132488 LC50 =	757.8403 LC25 =	
SLOPE = 39.95122	1.394177 LC50 =	121.8159 LC25 =	
	1.424625 LC50 =	386.4365 LC25 =	
	2.277929 LC50 =	99.05019 LC25 =	
SLOPE = 148.8525	. 2.91321 LC50 =	253.9342 LC25 =	
SLOPE = 5.685727	∨.7566037 LC50 =	44.3166 LC25 =	
SLOPE = 47.91444	1.021491 LC50 =	219.3803 LC25 =	
	1.602422 LC50 =	109.0636 LC25 =	
SLOPE = 130.1896	2.073583 LC50 =	275.612 LC25 =	
SLOPE = `9.6747	1.726019 LC50 =	319.22 LC25 =	
	· 1.44307 LC50 =	768.5995 LC25 =	
SLOPE = 68.97501	1.807582 LC50 =	163.0198 LC25 =	
SLOPE = 85-8454	1.262477 LC50=	· 294.0551~LC25 =	
SLOPE 245.4469	<del>2.1</del> 0449 LC50 =	513.9855-LC25-=	
SLOPE = 114.4296	1.469774 LC50 =	329.5386 LC25 =	
SLOPE = 250.6352	.9853856 LC50 =	1213.672 LC25 =	



## UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460

MAY 1 9 1997

OFFICE OF PREVENTION, PESTICIDES AND **TOXIC SUBSTANCES** 

SUBJECT: Review of acute testing of a freshwater fish study (GLN 72-1a) with

Fluroxypyr (DP Barcode: D23 ; ID No. 128959; MRID 440803-

07; Case no. 060640)

FROM:

John Simons, Environmental Scientist

Environmental Fate and Effects Division

THRU:

Elizabeth Leovey, Chief

Environmental Risk Characterization Branch

Environmental Fate and Effects Division

TO:

Joanne Miller, Project Manager

Registration Division

The Environmental Risk Branch II has completed the review of the data submitted by DowElanco for fluroxypyr for the purpose of registration. The following is a summary of the findings:

CITATION: Rick, D.L., et.al. 1996. Evaluation of the Acute Toxicity of Fluroxypyr 1-Methylheptyl ester to Bluegill, Lepomis macrochirus Rafinesque. Laboratory report ID: DECO-ES-3020. Laboratory: Environmental Toxicity Research Laboratory, Health and Environmental Sciences, the Dow Chemical Company, Midland, MI 48674. Sponsor: DowElanco.

CONCLUSIONS: This study is scientifically sound and adequate for fulfilling the guidelines for acute testing with a freshwater fish (GLN 72-1a). This study is classified as core.

## **RESULTS SYNOPSIS:**

LC50: >629 ai ug/L

NOEC: 629 ai ug/L

From the tests, it can be concluded that the 96-hour bluegill sunfish LC50 is greater than 629 ug/L, which is roughly six times the solubility of fluroxypyr. Because of the low solubility of fluroxypyr, no LC50 was determined.

Deviations: Although the study contained guideline deviations, the fact that there were no mortalities or observed effects makes these deviations less important because the deviations generally caused the fish greater stress. Deviations included: use of water that contained minimal chlorine, mean weight of fish below criteria, acclimation period less than recommended, total hardness outside recommended limits, and small size of aquaria.

If there are any questions, please contact John Simons (703) 305-6460.

DP Barcode : D230603

PC Code No : 128954

EEB Out

To:

Linda Propst

Product Manager 73

Special Review and Reregistration Division (H7508W)

Registration Division (H7505C)

From: John Simons, Environmentl Scientist

Environmental Risk Branch II/EFED (H7507C)

Attached, please find the EEB review of ...

Reg./File # 062719-EIL STARANE F

Chemical Name :\_\_\_ Fluroxypyr

Type Product Herbicide

Product Name <u>Technical</u>

Company Name DowElanco

Purpose Review the attached study submitted by

DowElanco in support of Section 3 registration

of the new chemical fluroxypyr

Action Code :\_\_010\_\_ Date Due

: <u>10/31/9</u>6

: John Simons Reviewer

Date In EEB: <u>10/17/96</u>

EEB Guideline/MRID Summary Table: The review in this package contains an evaluation of the following:

GDLN NO	MRID NO	CAT	GDLN NO	MRID NO	CAT	GDLN NO	MRID NO	CAT
71-1(A)			72-2(A)			72-7(A)		
71-1(B)			72-2(B)		·	72-7(B)		
71-2(A)	·	<u> </u>	72-3(A)			122-1(A)		
71-2(B)			72-3(B)			122-1(B)	<u> </u>	
71-3		·	72-3(C)			122-2		<u> </u>
71-4(A)			72-3(D)	· · · · · · · · · · · · · · · · · · ·		123-1(A)	<del></del>	
71-4(B)		<u> </u>	72-3(E)			123-1(B)		
71-5(A)		<u> </u>	72-3(F)			123-2		
71-5(B)			72-4(A)			124-1	· · · · · · · · · · · · · · · · · · ·	
72-1(A)	440803-07	Υ .	72-4 (B)			124-2		
72-1(B)		<u> </u>	72-5			141-1		
72-1(C)			72-6			141-2		
72-1(D)						141-5		

-Partial (Study partially fulfilled Guideline but additional information is needed; #-Supplemental (Study provided-useful information but Guideline was not satisfied); #-Unacceptable (Study was rejected)/Nonconcur

# DATA EVALUATION RECORD \$ 72-1(A) -- ACUTE LC<sub>50</sub> TEST WITH A WARMWATER FISH

1. CHEMICAL: FLUROXYPYR

PC Code No.: 1289

2. TEST MATERIAL: fluroxypyr 1-methyleptyl ester

<u>Purity</u>: 95.8%

3. CITATION

<u>Authors</u>: D.L. Rick, A.M. Landre, H.D. Kirk <u>Title</u>: Evaluation of the Acute Toxicity of

Fluroxypyr 1-Methylheptyl ester to

Bluegill, Lepomis macrochirus Rafinesque

Study Completion Date: March 11, 1996

Laboratory: Environmental Toxicity Research

Laboratory, Health and Environmental Sciences, The Dow Chemical Company,

Midland, MI 48674

Sponsor: DowElanco

Laboratory Report ID: DECO-ES-3020

MRID No.: 440803-07

DP Barcode: D230603 prid 1

4. REVIEWED BY: John Simons, Env. Scientist, EEB, EFED

Signature: ////

Date: 3/19/97

5. Peer Reviewed BY: Andrew Bryceland, Fishery Biologist, ERCB,

EFED

Signature:

Date: 3/19/97

6. STUDY PARAMETERS

Age or Size of Test Organism:

Juveniles

Definitive Test Duration:

96 hours

Study Method:

Static-renewal

Type of Concentrations:

Mean measured

#### 7. CONCLUSIONS:

This study is scientifically sound and adequate for fulfilling the guidelines for acute testing with a freshwater fish (GLN 72-1a). Although the study contained guideline deviations, the fact that there were no mortalities or observed sublethal effects makes these deviations less important because

the deviations generally caused the fish greater stress. The results of the tests are sufficient to conclude that the 96-hr bluegill sunfish LC50 is greater than 629 ai ug/L, which is roughly six times the solubility of fluroxypyr. Because of the low solubility of fluroxypyr, no LC50 was determined, and the LC50 value can not be categorically compared to LC50 values determined for other chemicals.

Results Synopsis

 $LC_{50}$ : >629 ai ug/L 95% C.I.: N/A

NOEC: 629 ai ug/L Probit Slope: N/A

#### 8. ADEOUACY OF THE STUDY

A. Classification: Core

- B. Rationale: Undissolved test material was observed in bottom of all aquaria (solubility = 109ug/L) in spite of dissolution aids, including acetone solvent and constant stirring, because the targeted dose level (100 ppm ai) greatly exceeded the solubility. Test water containing minimal chlorine (0.4 ppm) was used. However, LC50 of >629 ai PPB was observed and no mortalities or sublethal stress was observed.
- C. Repairability: N/A

#### 9. GUIDELINE DEVIATIONS

- 1. Use of water from treatment plant that contained "minimal" chlorine
- 2. Mean weight of test fish below criteria
- 3. Acclimation period of 7 days (vs 14 days required)
- 4. Total hardness of 65 mg/L as CaCO3 (vs 40-48 mg/L)
- 5. Inadequate size and fill volume of test aquaria
- 10. SUBMISSION PURPOSE: Registration

#### 11. MATERIALS AND METHODS

A. Test Organisms

Guideline Criteria	Reported Information
Species Preferred species is the bluegill sunfish (Lepomis macrochirus)	Blue gill sunfish (Leopomis macrochirus)
Mean Weight 0.5-5 g	0.318g
Mean Standard Length Longest not > 2x shortest	Mean: 25.0 mm Range:21-29 mm
Supplier	Northeastern Biologists, Rhinebeck, NY
All fish from same source?	Yes
All fish from the same year class?	Not reported

## B. Source/Acclimation

Guideline Criteria	Reported Information
Acclimation Period Minimum 14 days	Minimum 7 days
Wild caught organisms were quarantined for 7 days?	N/A
Were there signs of disease or injury?	Not reported
If treated for disease, was there no sign of the disease remaining during the 48 hours prior to testing?	N/A

Guideline Criteria	Reported Information
<b>Peeding</b> No feeding during the study	Last feeding 48 hours prior to testing
Pretest Mortality No more than 3% mortality 48 hours prior to testing	<3% mortality 5 days prior to testing.

# C. Test System

Guideline Criteria	Reported Information
Source of dilution water Soft reconstituted water or water from a natural source, not dechlorinated tap water	City of Midland water treatment plan. Water was chlorinated.
Does water support test animals without observable signs of stress?	Yes
Water Temperature 17pc or 22pc	17.3-17.8þC
pH Prefer 7.2 to 7.6	6.9-7.7
Dissolved Oxygen Static: p 60% during 1 <sup>st</sup> 48 hrs and p 40% during 2 <sup>nd</sup> 48 hrs, flow-through: p 60%	Static: 0-48 hrs. >78% saturation 48-96 hrs. >38 saturation
Total Hardness Prefer 40 to 48 mg/L as CaCO <sub>3</sub>	65 mg/L as CaCO₃

Guideline Criteria	Reported Information
Test Aquaria  1. Material: Glass or stainless steel 2. Size:	1. Glass 2. 12 L 3. 10 L
Volume of 19 L (5 gal) or 30 x 60 x 30 cm 3. Fill volume: 15-30 L of solution	•
Type of Dilution System  Must provide reproducible supply of toxicant	Static-renewal
Flow Rate  Consistent flow rate of 5- 10 vol/24 hours, meter systems calibrated before study and checked twice daily during test period	N/A
Biomass Loading Rate Static: p 0.8 g/L at p 17pC, p 0.5 g/L at > 17pC; flow- through: p 1 g/L/day	0.318 g/L at 17.3-17.8oC
Photoperiod 16 hours light, 8 hours dark	16 hours light, 8 hours dark
Solvents Not to exceed 0.5 ml/L for static tests or 0.1 ml/L for flow-through tests	Solvent: acetone Maximum conc.: 0.5 ml/L.

## D. Test Design

Guideline Criteria	Reported Information
GOLDET DE LECELO	repozeca zwzoranaczon
Range Finding Test  If LC <sub>50</sub> >100 mg/L with 30  fish, then no definitive  test is required.	Not required
Nominal Concentrations of Definitive Test Control & 5 treatment levels; dosage should be 60% of the next highest concentration; concentrations should be in a geometric series	100 mg ai/L used for all tests with no observed effect
Number of Test Organisms Minimum 10/level, may be divided among containers	30 divided into 10 each test
Test organisms randomly or impartially assigned to test vessels?	yes
Biological observations made every 24 hours?	Not reported
Water Parameter  Measurements  1. Temperature  Measured constantly  or, if water baths  are used, every 6  hrs, may not vary >  1pC  2. DO and pH  Measured at beginning  of test and every 48  h in the high,  medium, and low doses and in the control	Temperature measured constantly in one aquaria. Did not vary >1oC. Temperature, D.O. and pH were measured in all test vessels at 0, 48, and 96 hrs.

Guideline Criteria	Reported Information
Chemical Analysis Needed if solutions were aerated, if chemical was volatile, insoluble, or known to absorb, if precipitate formed, if containers were not steel or glass, or if flowthrough system was used	Control and treatment were sampled for total test substance. Samples taken while aquaria were stirred and from filtration of sample. Most test compound remained undissolved.  Concentrations were determined by HPLC.

## 12. REPORTED RESULTS

## A. General Results

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes
Recovery of Chemical	46.2-61.7% day four
Control Mortality Not more than 10% control organisms may die or show abnormal behavior.	0.0% mortality
Raw data included?	Yes

Guideline Criteria	Reported Information
Signs of toxicity (if any) were described?	N/A

Mortality

Concentration (ppm)		Num ber of Fis	Cumulative Number Dead			
Nomin al Mean			Hour of Study			
	Measur ed	ħ	24	48	72	96
Contr Ol	-	10	0.	0	0	C
100	0.629	0	0	0	0	.0

Other Significant Results: None

## B. Statistical Results

Method:

96-hr LC<sub>50</sub>: >629 PPB ai Probit Slope: N/A 95% C.I.: N/A

NOEC: 629 PPB ai

13. VERIFICATION OF STATISTICAL RESULTS N/A

#### 14. REVIEWER'S COMMENTS:

Undissolved test material was observed in all aquaria, in spite of use of solvent and stirring. Under these conditions the concentrations to which fish were exposed might have been over estimated. To account for this, test solutions were filtered and a mean soluble fluroxypyr was determined to be 629 ug/L, which may be considered to be the bioavailable component. The LC50 is greater than 629 ug/L.

Table 4: Evaluation of the Acute Toxicity of Fluroxypyr 1-MHE to the Bluegill. Summarized Results from Analysis of 99.0 mg/L Test Solutions.

	Summary of M	leasured Concen	itrations of Test	Solutions (a)	·
Nominal Concentration = 99.0 m	g/L Fluroxypyr 1-MH	E			
	Avera	L) (b)			
	Dose Solution A  Day 0-1	Mean and % of Nominal Values			
		•			
Total Fluroxypyr 1-MHE				•	
Average:	41.4	. 60.7	63.6	56.6	Mean = 55.6
Standard deviation:	6.4	13.2	30.5	36.6	% of Nominal = 56.2 %
Soluble Fluroxypyr 1-MHE	·				
Average:	0.590	0.549	0.745	0.632	Mean = 0.629
Standard deviation:	0.067	0.114	0.158	0.105	% of Nominal = 0.6 %
Fluroxypyr acid.			•		
Average:	0.303	0.295	0.305	0.331	Mean = 0.309
Standard deviation:	0.019	0.025	0.011	0.029	% of Nominal = 0.3 %
				·	

<sup>(</sup>a) Results from 99 mg/L treatment vessels only; control samples were all below the limit of quantitiation.

<sup>(</sup>b) Values for Fluroxypyr acid expressed as molar equivalent Fluroxypyr 1-MHE concentration.

## UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

John J. Jachetta, Ph.D. Dow AgroSciences LLC 9330 Zionsville Road Indianapolis, IN 46268 MAY 28 1998

Dear Dr. Jachetta:

Subject:

Fluroxypyr - Application for Pesticide Registration

Starane F (EPA File Symbol 62719-EIL) Starane EC (EPA File Symbol 62719-EIA)

EPA Petition No. 6F4772

Your Submission Dated August 6, 1996

The Agency has completed additional reviews of the application for pesticide registration referenced above. The following comments apply regarding the environmental fate and effects data provided with this application:

- Available data indicates that the use of fluroxypyr will pose minimal risk to terrestrial animals and aquatic animals and plants, including threatened and endangered species. However, available data indicates that the use of fluroxypyr will pose a high risk to terrestrial plants, and may harm threatened and endangered species of terrestrial plants.
- 2) Additional ecological effects data have been reviewed and evaluated. It has been determined that data gaps exist in the phytotoxicity studies submitted for fluroxypyr. A complete copy of the review dated January 22, 1998 is included with this letter to provide the specific data gaps for each unacceptable study and the reasons for these conclusions.
- 3) Environmental fate and transport data has been reviewed and evaluated. It has been determined that data gaps exist in the areas of soil mobility (§163-1), terrestrial field dissipation (§164-1), and bioaccumulation in fish (§165-4). A complete copy of the review dated March 31, 1998 is included with this letter to provide the specific data gaps for each unacceptable study and the reasons for these conclusions.

DK; 30	5-7546!	48/PM2	-3 cc	ONCURRENCES			
SYMBOL .	7505C						
SURNAME .	D. KENNY						<i>~</i> .
DATE •	5/28/98					·	ż

We will await your response to the data deficiencies cited above. You will be notified upon the completion of the remaining reviews still pending with this application for pesticide registration.

Sincerely yours,

Joanne I. Miller Product Manager (23) Herbicide Branch Registration Division (7505C)

Enclosures

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Table 1. Estimated Environmental Concentrations on Avian and Mammalian Food Items (ppm) Following a Single Application at 1 lb ai/A

Food Items	EEC (ppm) Predicted Maximum Residue <sup>1</sup>	EEC (ppm) Predicted Mean Residue <sup>t</sup>
Short grass	240	85
Tall grass	110	36
Broadleaf/forage plants, and small insects	135	45
Fruits, pods, seeds, and large insects	15_	7

<sup>&</sup>lt;sup>1</sup> Predicted maximum and mean residues are for a 1 lb ai/a application rate and are based on Hoerger and Kenaga (1972) as modified by Fletcher et al. (1994).

#### b. Surface Water

EFED calculates EECs using the <u>GEN</u>eric <u>Expected Environmental Concentration</u>
Program (GENEEC). The EECs are used for assessing acute and chronic risks to aquatic organisms. Acute risk assessments are performed using peak EEC values for single and multiple applications. Chronic risk assessments are performed using the 21-day EECs for invertebrates and 56-day EECs for fish.

The GENEEC program uses basic environmental fate data and pesticide label application information to estimate of the expected EECs following treatment to 10 hectares. The model calculates the EEC of a pesticide in a one hectare, two meter deep pond, taking into account the following: (1) adsorption to soil or sediment, (2) soil incorporation, (3) degradation in soil before washoff to a water body, and (4) degradation within the water body. The model also accounts for direct deposition of spray drift into the water body (assumed to be 1% and 5% of the application rate for ground and aerial applications, respectively). This model was run using two applications with an interval between applications of 120 days. The environmental fate parameters used in the model were:

mean soil  $K_{OC}$ . 50 (minimum reported value) solubility: 0.90 mg/L

aerobic soil metabolism half-life:

23 days (maximum of 4 reported values)

aerobic aquatic metabolism half-life: 14 days hydrolysis half-life (@ pH 7): stable (454 days) aqueous photolysis half-life (@ pH 7): stable

The results of the GENEEC model are reported below.

Estimated Environmental Concentrations (EECs) for Broadcast Applications

Use Site	Application Method	Application Rate (lbs ai/A)	Number of Applications	Initial (Peak) EEC (ppb)	21-day average EEC (pph)	56-day average EEC (ppb)
Wheat, Barley, and	Unincorporated ground spray	0.125	1	5.60	3.54	1.92
Oats	Aerial spray <sup>2</sup>	0.125	1	5,60	3.56	1.93
Uncultivated Areas and Volunteer Potato	Unincorporated ground spray	0.25	1 .	11.2	7.08	3.84
Control in Wheat, Barley, and Oats	Aerial spray	0.25 .	1	11.2	7.12	3.86

<sup>1</sup> Spray drift is assumed to be 1% of the application rate.

## 3. Ecological Toxicity Data

## a. Toxicity to Terrestrial Animals

## i. Birds, Acute and Subacute

An acute oral toxicity study using the technical grade of the active ingredient (TGAI) is required to establish the toxicity of fluroxypyr acid and fluroxypyr MHE to birds. Results show that fluroxypyr acid and fluroxypyr MHE are practically nontoxic to birds on an acute oral basis (Table 2).

Table 2. Acute Oral Toxicity of Fluroxypyr to Birds

Species	% ai	LD50 (mg ai/kg)	Toxicity Category	MRID No. Author/Year	Study Classification <sup>1</sup>
· · · · · · · · · · · · · · · · · · ·			Fluroxypyr Acid		
Northern bobwhite quail (Colinus virginianus)	98.8	>2000	Practically nontoxic	40244515 Roberts and Phillips, 1984	Supplemental <sup>2</sup>
Mallard duck (Anas platyrhynchos)	Not reported	>2000	Practically nontoxic	40244514 Roberts and Phillips, 1984	Core
<del></del>			Fluroxypyr MHE		
Northern bobwhite quail (Colinus virginianus)	Not reported	>2000	Practically nontoxic	40244546 Roberts and Phillips, 1984	Core
Mallard duck (Anas platyrhynchos)	98.6	>2000	Practically nontoxic	40244516 Roberts and Phillips, 1983	Core

<sup>1</sup> Core (study satisfies guideline). Supplemental (study is scientifically sound, but does not satisfy guideline)

Subacute dietary studies using the TGAI are required to establish the dietary toxicity of fluroxypyr acid and fluroxypyr MHE to birds. Studies with an upland game bird and a waterfowl are required. Results indicate that fluroxypyr acid and fluroxypyr MHE are practically nontoxic

<sup>2</sup> Spray drift is assumed to be 5% of the application rate.

<sup>2</sup> Only three concentrations were tested, whereas at least five are required.

to birds on a subacute dietary basis (Table 3). In each study, no mortality was observed at the highest test concentration.

Table 3. Subacute Dietary Toxicity of Fluroxypyr to Birds

Species	% ai	5-Day LC50 (ppm) <sup>1</sup>	Toxicity Category	MRID No. Author/Year	Study Classification
			Fluroxypyr Acid		
Mallard duck (Anas platyrhynchos)	98.3	>5620	Practically nontoxic	42137302 Grimes, Lynn, and Smith, 1991	Core
Northern bobwhite (Colinus virginianus)	Not reported	>5000	Practically nontoxic	40244547 Roberts and Phillips, 1983	Core
-			Fluroxypyr MHE		
Mallard duck (Anas platyrhynchos)	99.1	>5620	Practically nontoxic	42137301 Grimes and Jarber, 1988	Core
Northern bobwhite (Colinus virginianus)	Not reported	>5000	Practically nontoxic	40244517 Roberts and Phillips, 1983	Core

<sup>&</sup>lt;sup>1</sup> Test organisms observed an additional three days while on untreated feed.

#### ii. Birds, Chronic

Avian reproduction studies using the TGAI are required for [both forms of] fluroxypyr because the following conditions are met: [(1) birds may be subject to repeated or continuous exposure to the pesticide, especially preceding or during the breeding season, (2) the pesticide is stable in the environment to the extent that potentially toxic amounts may persist in animal feed. (3) the pesticide is stored or accumulated in plant or animal tissues, and/or, (4) information derived from mammalian reproduction studies indicates reproduction in terrestrial vertebrates may be adversely affected by the anticipated use of the product.] The preferred test species are mallard duck and bobwhite quail.

Testing with fluroxypyr MHE show that dietary concentrations of 500 ppm can cause an impairment of eggs production in some birds (Table 4). The no-observable-effect concentration for fluroxypyr MHE is 250 mg ai/kg BW.

Table 4. Reproduction Toxicity of Fluroxypyr MHE to Birds

Species	% ai	NOEC (ppm ai)	LOEC (ppm ai)	LOEC Endpoints	MRID No. Author/Year	Study Classification
Northern bobwhite (Colinus virginianus	.99.1	1000	Not determined	None	42137303 Beavers, Hawtrot, and Jaber, 1989	Core
Mallard (Anas platyrhynchos)	99.1	250	500	Reduced egg production	42137304 Beavers, Hoxter, Nichols, Hawrot, and Jaber, 1989	Core

### iii. Mammals, Acute and Chronic

Rat toxicity data obtained from the Agency's Health Effects Division (HED) was substituted for wild mammal testing for assessing acute and chronic effects on mammals.

A single-dose oral LD<sub>50</sub> study (MRID 44080329) was performed in which fluroxypyr MHE (25.6% pure) was administered to the laboratory rat (*Rattus norvegicus*). The LD<sub>50</sub> was 3740 mg/kg for males and 3160 mg/kg for females. The geometric mean of the values for males and females was 3440 mg/kg. Correcting for the lack of purity, this mean corresponds to 880 mg ai/kg. This classifies fluroxypyr MHE as slightly toxic to small mammals on an acute oral basis.

Chronic toxicity data for mammalas are given in Table 5. Fluroxypyr MHE produces chronic toxic effects in mammals only at very high dietary concentrations. For the purpose of assessing the risk of chronic ecological effects in mammals, the NOEL is 2000 ppm and the LOEL is 10,000 ppm.

Table 5. Chronic Mammalian Toxicity for Fluroxypyr MHE

Species	% ai	Test Type	Endpoint	NOEL (ppm)	LOEL (ppm)	MRID No.
Laboratory rat (Ratius norvegicus)	99.0	2-generation reproduction	Systemic effects (Renal damage)	2000	10.000	44080321
			Reproduction	15,000	ND	
		•	Pup survival and weight gain	10,000	20.000	
Rabbit	95.8	Developmental	Maternal/ developmental effects (increased abortions)	16,700	33,300	44080319

#### iv. Insects

A honey bee acute contact study using the TGAI is required for fluroxypyr because its use on uncultivated areas will result in honey bee exposure. Results of honey bee toxicity tests indicate that fluroxypyr acid and fluroxypyr MHE are practically nontoxic to bees on an acute contact basis (Table 6).

Table 6. Acute Contact Toxicity to Nontarget Insects

Species	% ai	LD50 (µg/bee)	Toxicity Category	MRID No. Author/Year	Study Classification
			Fluroxypyr Acid		
Honey bee (Apis mellifera)	98.3	-25	Relatively nontoxic	42137314 Lynn and Hoxter, 1991	Core
		·. · · · · · · · · · · · · · · · · · ·	Fluroxypyr MHE		
Honey bee (Apis mellifera)	98.5	>25	Relatively nontoxic	42137313 Lynn and Hoxter, 1991	Core
Honey bee (Apis mellifera)	97	Not determined	Not determined	40244527 Cole 1983	Supplemental

## b. Toxicity to Freshwater Aquatic Animals

## i. Freshwater Fish, Acute

Two freshwater fish toxicity studies using the TGAI are required to establish the toxicity of fluroxypyr to fish. The preferred test species are rainbow trout (a coldwater fish) and bluegill sunfish (a warmwater fish). Results of these tests are given in Table 7.

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Table 7. Acute Toxicity of Fluroxypyr to Freshwater Fish

Species, Test Type (Flow-through or Static)	<u>% ai</u>	96-hour LC50 (mg ai/L)	Toxicity Category	MRID No. Author/Year	Study Classification
· · · · · · · · · · · · · · · · · · ·		Flu	гохурут Acid		
Rainbow trout (Oncorhynchus mykiss), static	99	>100	Practically nontoxic	40244518 Willis	Core
Bluegill sunfish ( <i>Lepomis macrochirus</i> ), static	98.8	14.3	Slightly toxic	42137306 Weinberg, Richardson, Rick, and Piasecki, 1991	Core
Golden Orfe (Leuciscus idus)	99	>100	Practically nontoxic	40244519 Wallis 1984	Supplemental
Rainbow trout (Oncorhynchus mykiss), flow through	unknown	13.4	Slightly toxic	40244525	Supplemental
		Flur	охурут МНЕ		
Rainbow trout (Oncorhynchus mykiss), static	98.5	>0.11	Not determined <sup>t</sup>	42137307 Weinberg, Richardson. Rick, and Piasechi. 1991	Core
Rainbow trout (Oncorhynchus mykiss), static	Technical	>0.7	Not determined <sup>1</sup>	40244522 Willis	Core
Bluegill sunfish ( <i>Lepomis macrochirus</i> ). static	95.8	>0.63	Not determined <sup>2</sup>	44080307	Core
Golden Orfe (Leuciscus idus)	Not reported	>0.7	Not determined <sup>1</sup>	40244523 Wallis, 1984	Supplemental
Bluegill sunfish ( <i>Lepomis macrochirus</i> ), static				42137305	Invalid

<sup>1</sup> Test concentrations up to the solubility limit caused no mortality.

Since the  $LC_{50's}$  for the bluegill sunfish fall in the range of 10 to 100 ppm, fluroxypyr acid is considered slightly toxic to freshwater fish on an acute basis. Acute toxicity tests failed to determine  $LC_{50}$ 's for fluroxypyr MHE because motality did not occur when tested up to the solubility limit. Since fluroxypyr MHE is not acutely toxic at its solubility limit, it is also considered practically nontoxic to freshwater fish on an acute basis.

A degradation product of fluroxypyr is pyridinol. Wan et al. (1987) found that the 96-hr  $LC_{50}$  of pyridinol for juveniles of six salmonid species ranged from 1.5 to 2.7 mg/L. This classifies pyridinol as moderately toxic to fish on an acute basis.

#### ii. Freshwater Fish, Chronic

Because of the low acute toxicity to freshwater fish, early life-stage and fish life-cycle

<sup>2</sup> A test concentration at the solubility limit cause no mortality.



## UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES, AND TOXIC SUBSTANCES

#### **MEMORANDUM**

SUBJECT: Review for Section 3 Registration of Fluroxypyr Acid (Chemical #

128959) and Fluroxypyr MHE (Chemical # 128968-5) (ID # 062719-EIL SRARANE F, Case # 060640, Bar Code # D236845 and D231718)

FROM:

F. Nicholas Mastrota and William R. Effland

Environmental Risk Branch II

F. Nicholas Mastrola 3/3 Environmental Fate and Effects Division 7507C

THRU:

Elizabeth M. Leovey, Chief

Environmental Risk Branch II

Environmental Fate and Effects Division 7507C

TO:

Joanne Miller (23)

Registration Division (7505C)

Attached is EFED's review for the Section 3 use of fluroxypyr MHE (128968-5) to control broadleaf weeds and perennials in wheat, barley, oats, and miscellaneous uncultivated areas. Fluroxypyr MHE is the ester form of fluroxypyr acid (128959). The registrant of fluroxypyr is DowElanco.

#### Summary of Risks

EFED concludes that use of fluroxypyr MHE will pose minimal risk to terrestrial animals and aquatic animals and plants, including threatened and endangered species. However, risk quotients indicate that all uses of fluroxypyr MHE will pose a high risk to terrestrial plants, and may harm threatended and endangered species of terrestrial plants. The predominant risk if from exposure of foliage to spray drift. Risk quotients for ground applications only marginally exceed the LOC, indicating a relatively minor risk. For aerial applications, risk is greater due to the greater amount of spray drift. For this exposure, risk quotients were 5.2 for wheat, oats, and barley and 10 for other uncultivated use sites, as well as volunteer potato control in wheat, barley, and oats. The standard label recommendations for reducing spray drift would help to mitigate this risk.



# UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460

#### OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

#### **MEMORANDUM**

SUBJECT:

Review for Section 3 Registration of Fluroxypyr Acid (Chemical # 128959)

and Fluroxypyr MHE (Chemical # 128968-5)

(STARANE EC, Case # 060640, Bar Code # D236845 and D231718)

TO:

Joanne Miller (23)

Registration Division (7505C)

FROM:

F. Nicholas Mastrota, Ph.D., Biologist

William R. Effland, Ph.D., Soil Scientist

Environmental Risk Branch II

Environmental Fate and Effects Division 7507C

THROUGH:

Elizabeth M. K. Leovey, Ph.D., Chief

Environmental Risk Branch II

Environmental Fate and Effects Division 7507C

Attached is EFED's review for the Section 3 use of fluroxypyr MHE (128968-5) submitted by the registrant, Dow Agrosciences. Fluroxypyr MHE is the ester form of fluroxypyr acid (128959). Fluroxypyr-MHE (Starane\* EC) is proposed as a selective, post-emergent herbicide for control of annual and perennial broadleaf weeds in small grains (wheat, oats, barley), fallow cropland and non-cropland.

#### A. Executive Summary of Risk Characterization

#### 1. General Risk Characterization

EFED concludes that use of fluroxypyr MHE will pose minimal risk to terrestrial and aquatic animals, including threatened and endangered species. The available data indicate that risk to aquatic plants is also minimal, but this conclusion is uncertain because acceptable toxicity data with a freshwater diatom are outstanding. Risk quotients indicate that all uses of fluroxypyr MHE

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will pose a high risk to terrestrial plants, and may harm threatended and endangered species of terrestrial plants. The predominant risk is from exposure of foliage to spray drift. Risk quotients for ground applications only marginally exceed the LOC, indicating a relatively minor risk. For aerial applications, risk is greater due to the greater amount of spray drift. For this risk assessment, risk quotients were 5.2 for applications to wheat, oats, and barley and 10 for other uncultivated use sites, as well as volunteer potato control in wheat, barley, and oats. The standard label recommendations for reducing spray drift should help mitigate this risk.

Although fluroxypyr acid is classified as mobile to very mobile in the laboratory studies, dissipation by hydrolysis and microbial degradation reduced persistence and limited downward transport (i.e., leaching) in the submitted field studies.

Additional environmental fate and phytotoxicity data are needed to adequately assess the risks of the degradation products of fluroxypyr.

## B. Outstanding Data Requirements

#### 1. Ecological Effects

Data requirements are outstanding for the following ecological effects studies:

Guideline	Study Type	Test Species
123-1 (a)	Seedling Emergence Phytotoxicity Test with Fluroxypyr Acid	Three monocots, other than corn, that represent two families, and five dicots, other than radish
123-2	Aquatic Plant Growth and Reproduction Test	A freshwater diatom

Additional phytotoxicity testing is required with fluroxypyr acid because fluroxypyr MHE is expected to rapidly degrade into fluroxypyr acid through base-catalyzed hydrolysis and microbial-mediated metabolism, and because supplemental data indicates that fluroxypyr acid has greater phytotoxicity than the parent compound, fluroxypyr MHE. Vegetative vigor testing is not required for the acid form because exposure to vegetation would be to the parent, fluroxypyr MHE. Supplemental data submitted to the Agency (MRID 44094902) were sufficient as a tier I study for effects of fluroxypyr acid on seedling emergence. These data indicate that application of fluroxypyr acid at rates up to 0.25 lb ai/A causes less than 25% inhibition of emerging seedlings for only two species, corn and radish. Tier II testing is required for eight additional test species, as described in the above table.

The registrant submitted an aquatic plant toxicity test with *Navicula pelliculosa* (MRID 44080339) that was invalid. A new study is required to establish the toxicity of fluroxypyr MHE to a freshwater diatom and fulfill guideline number 123-2.

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## 2. Environmental Fate and Transport

The soil mobility data requirement (163-1) is not currently satisfied. Information on the mobility of the major degradates, dichloropyridinol and methoxypyridine, is not acceptable at this time.

Information on the vapor pressure and Henry's Law Constant of the degradate, dichlorpyridinol, is requested to adequately characterize its potential to volatilize.

The terrestrial field dissipation data requirement (164-1) is not satisfied at this time because adequate storage stability data were not submitted for soils collected from the test sites. The data requirement is upgradeable with the submission of acceptable soil storage stability data for fluroxypyr MHE, fluroxypyr acid, and major degradates using soils obtained from the respective test sites.

The bioaccumulation in fish data requirement (165-4) is not satisfied at this time because the submitted study does not provide adequate information on the bioaccumulation of fluroxypyr-MHE or fluroxypyr acid in fish.

#### EFED/ERB II Task Team Members:

William R. Effland, Ph.D., Soil Scientist, Environmental Fate and Water Resources Assessment

Nicholas M. Mastrota, Ph.D., Wildlife Biologist, Ecological Effects

Andrew Bryceland, Fisheries Biologist (Peer review)

James Breithaupt, Agronomist (Peer review)

Attachments:

Electronic copies (via cc:Mail)

Thomas Bailey Joseph J. Merenda Mah Shamim

Elizabeth Leovey

Denise Keehner Arnet Jones Daniel Rieder

Doug Urban

Betsy Grim

#### 1. Environmental Fate and Transport Assessment

## A. Environmental Fate for Fluroxypyr

Degradation of fluroxypyr-MHE in environmental fate laboratory studies occurs through base-catalyzed hydrolysis and microbial-mediated metabolism under aerobic conditions. In sterilized buffered water, fluroxypyr-MHE transformed to fluroxypyr acid by base-catalyzed hydrolysis with a half-life of 3 days at pH 9. Hydrolysis of fluroxypyr-MHE was not observed in the acidic test system at pH 5 and it was essentially stable at pH 7 with an extrapolated half-life of 454 days. Both fluroxypyr-MHE and fluroxypyr acid do not degrade by photolysis in aqueous environments. Fluroxypyr-MHE does not significantly degrade via photolysis on soil. Fluroxypyr-MHE and fluroxypyr acid transform rapidly in aerobic soil environments. In the aerobic soil metabolism study, microbial degradation of fluroxypyr-MHE appears to follow a biphasic degradation pattern with an initial first-order half-life of 1 to 3 weeks in four test soils. The rate of metabolism decreased significantly after 2 months. Degradation of fluroxypyr-MHE yields fluroxypyr acid (with herbicidal activity), 4-amino-3,5-dichloro-6-fluoro-pyridin-2-ol (pyridinol metabolite). 4-amino-3,5-dichloro-6-fluoro-2-methoxypyridine (methoxypyridine metabolite) and CO<sub>2</sub>.

The laboratory studies assessing the aquatic metabolism of fluroxypyr-MHE and fluroxypyr acid indicate transformation of fluroxypyr-MHE to fluroxypyr acid via biotic hydrolysis and subsequent metabolism of fluroxypyr acid to mono- and dichloro-substituted pyridinol degradates. Fluroxypyr-MHE and fluroxypyr acid degrade with an estimated half-life of 14 days in the aerobic aquatic environment. In the anaerobic aquatic environment with sediment, both fluroxypyr-MHE and fluroxypyr acid transformed with an estimated half-life of 8 days to 3-chloropyridinol and dichloropyridinol degradates. The methoxypyridine metabolite was not reported in either laboratory aquatic metabolism study.

Fluroxypyr acid is considered mobile to very mobile in soil based on Freundlich K<sub>ads</sub> values ranging from 0.11-1.9 ml/g with four test soils (silt loam, sandy loam, loam, and silty clay textures). These soil/water partitioning coefficients indicate fluroxypyr will occur principally in the aqueous phase of soil/water environmental systems. Results of batch equilibrium studies with fluroxypyr-MHE (single point concentration of 0.066 mg/L) yielded K<sub>d</sub> values (ml/g) of 260 in a silt loam; 95 in sandy loam, 190 in loam and 210 in silty clay soil:solution slurries equilibrated for 10 minutes. However, the soil mobility data requirement (163-1) is not currently satisfied. Information on the mobility of the primary degradates of fluroxypyr acid, dichloropyridinol and methoxypyridine, is not acceptable at this time.

Based on the reported vapor pressure and estimated Henry's law Constant, fluroxypyr-MHE and fluroxypyr acid are not predicted to readily volatilize from soil or water; therefore, volatilization is not considered a significant route of dissipation. Information on the vapor pressure and Henry's Law Constant of dichlorpyridinol is requested to adequately characterize its volatilization potential.

Fluroxypyr residues were slightly persistent in terrestrial field dissipation studies conducted at

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three locations in the United States. Total fluroxypyr residues (fluroxypyr MHE plus fluroxypyr) dissipated in Putnam silty clay loam (Missouri), Gardena sandy clay loam (North Dakota), and Quincy loamy sand (Washington) soils with registrant-calculated half-lives of 24.8, 36.3, and 13.2 days, respectively in plots vegetated with spring wheat. Results from these terrestrial field dissipation studies and supporting laboratory environmental fate data suggest fluroxypyr-MHE and fluroxypyr acid dissipated principally by base-catalyzed hydrolysis and microbial-mediated metabolism. The rate of dissipation limited downward transport (i.e., leaching) in the submitted field studies.

The terrestrial field dissipation data requirement (164-1) is not satisfied at this time because adequate storage stability data were not submitted for soils collected from the test sites. The soil used in the storage stability study was not representative of the soils found at the test sites, particularly in ND and WA. This study may be upgraded with the submission of acceptable frozen storage stability data for fluroxypyr MHE, fluroxypyr (acid), and metabolites using soils obtained from the respective test sites.

#### B. Environmental Fate Data Summaries.

#### Hydrolysis (161-1)

The abiotic hydrolysis of fluroxypyr-MHE is base-catalyzed and results in the formation of fluroxypyr acid. At pH levels between 5 and 7, hydrolysis is not an important degradation process. Fluroxypyr-MHE was stable to abiotic hydrolytic degradation at pH 5 and degraded very slowly at pH 7 with an extrapolated half-life of 454 days (30-day study duration). At pH 9, fluroxypyr-MHE degraded rapidly to fluroxypyr acid; the half-life for fluroxypyr-MHE was 3.2 days. The data requirement (161-1) is satisfied. (MRID #40244539)

#### Photodegradation in Water (161-2)

Both fluroxypyr-MHE and fluroxypyr acid do not degrade by photolysis in sterile aqueous environments. Radiolabeled [2,6-14C]fluroxypyr MHE, at 0.051 ppm, was stable and did not degrade photolytically (registrant-calculated, extrapolated half-life of 197 days) in pH 5 sodium phosphate buffer solution that was irradiated with natural sunlight at approximately 25° C for 34 days. In a supplemental study, [2,6-14C]fluroxypyr MHE appeared to be stable (registrant-calculated, extrapolated half-life of 552 days) in natural water (collected from Brewer Lake, ND) irradiated for 28 days under similar conditions. Radiolabeled [2,6-14C]fluroxypyr acid, at 0.044 ppm, was stable to photolytic degradation (registrant-calculated, extrapolated half-life of 429 days) in pH 5 sodium phosphate buffer solution that was irradiated with natural sunlight at approximately 25 °C for 34 days. The data requirement (161-2) is satisfied. (MRID #44080342)

#### Photodegradation on Soil (161-3)

Fluroxypyr-MHE does not significantly degrade via photolysis on soil. Radiolabeled [2,6-14C]fluroxypyr MHE, at a treatment rate of 4 mg/cm<sup>2</sup>, degraded with a registrant-reported.

extrapolated half-life of 152.7 days on air-dried (5.9% moisture content) clay loam soil sample (Barnes loam series) incubated at approximately 25° C for 30 days in natural sunlight. Using the average fluroxypyr-MHE percent of the applied radioactivity data, the extrapolated half-life was recalculated to be 119 days ( $r^2 = 0.88$ , n = 6; first-order linear regression analysis) for the air-dried soil experiment. The discrepancy between half-life estimates should not affect the validity of the study since fluroxypyr-MHE does not significantly photodegrade on soil. The data requirement (161-3) is satisfied (MRID #44080343)

## Aerobic Soil Metabolism (162-1)

Fluroxypyr-MHE and fluroxypyr acid transform rapidly in aerobic soil environments. In the laboratory aerobic soil metabolism studies, fluroxypyr-MHE, applied at ≈2.0 mg/kg, transformed via biotic hydrolysis to fluroxypyr acid. The registrant-calculated half-lives of 12, 23, 13 and 7 days in Catlin silt loam, Hanford sandy loam, Barnes loam and Mhoon silty clay soils, respectively, were determined for selected data from flasks incubated in the dark at 26° C for up to 365 days. The characteristics of the test soils are listed in Table AA.

In aerobic soil, fluroxypyr acid degraded to 4-amino-3,5-dichloro-6-fluoro-pyridin-2-ol (pyridinol metabolite), 4-amino-3,5-dichloro-6-fluoro-methoxypyridine (methoxypyridine metabolite) and carbon dioxide. The pyridinol metabolite reached a maximum of 2.8-18.7% of the applied at 7-56 days posttreatment and the methoxypyridine metabolite was 4.3-38.2% of the applied at 28-100 days posttreatment. Carbon dioxide totaled 46.8-76.2% of the applied radioactivity and unextractable radioactivity increased to a maximum of 5.0-13.2% at 100-365 days posttreatment. The data requirement (162-1) is satisfied. (MRID #42137317)

Table AA. Soil Properties

Soil Series	Subgroup	State	рН	ОС	CEC	Sand	Clay
				(%)	(meq/100 g)	(%)	(%)
Catlin silt loam	Typic Argiudolls	IL	5.9	2.23	15.0	16	24
Hanford sandy loam	Typic Xerorthents	CA	7.5	0.22	5.2	64	10
Barnes loam	Udic Haploborolls	ND	6.8	3.08	15.9	40	22
Mhoon clay	Typic Fluvaquents	MS	7.0_	1.26	18.8	14	46

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## Anaerobic Aquatic Metabolism (162-3)

In the anaerobic aquatic environment with sediment, both fluroxypyr-MHE and fluroxypyr acid are rapidly transformed to 3-chloropyridinol and dichloropyridinol degradates. Total fluroxypyr [pyridine ring-labeled [14C-2,6] fluroxypyr MHE plus fluroxypyr acid], tested at 0.1 µg/mL (as fluroxypyr MHE), degraded with a registrant-calculated half-life of 8 days (0 to 4 week data) in anaerobic flooded silt loam sediment that was incubated in darkness at 25°C for up to 12 months. Two major degradates were identified:

4-amino-3-chloro-6-fluro-2-pyridinol (3-chloropyridinol; 21.5% of the applied at 12 months posttreatment); and

4-amino-3,5-dichloro-6-fluro-2-pyridinol (dichloropyridinol; 44.5% of the applied at 12 months posttreatment).

Unextracted [14C]residues comprised 27.8% of the applied at 12 months posttreatment. The majority of [14C]residues (maximum of 82.3% of the applied at 4 months posttreatment) were observed in the water phase. Radiolabeled 14CO<sub>2</sub> accounted for only 1.2% of the applied radioactivity at 12 months posttreatment. The data requirement (162-3) is satisfied. (MRID #44080344)

#### Aerobic Aquatic Metabolism (162-4)

Fluroxypyr-MHE and fluroxypyr acid degrade rapidly in the aerobic aquatic environment. In the laboratory, total fluroxypyr [pyridine ring-labeled [14C-2,6] fluroxypyr MHE plus fluroxypyr (acid)], at a nominal concentration rate of 0.1 µg/ml (as fluroxypyr MHE), degraded with a registrant-calculated half-life of 5.1 days (0 to 4 week data) in aerobic flooded silt loam sediment that was incubated in darkness at 25 °C for up to 12 months. Using the concentration data through the 60-day study period, the aerobic aquatic half-life was estimated to be 14 days [assumed first-order regression of the natural logarithm of the percent of the applied radioacitivity data vs. time (days)]. The 14-day half-life estimate was used in Tier 1 (GENEEC) surface water modeling.

Fluroxypyr acid (4-amino-3,5-dichloro-6-fluoro-pyridyloxyacetic acid) was a maximum of 30.9% of the applied at 1 week posttreatment, and decreased to 0.8-1.5% of the applied at 4 weeks through 2 months posttreatment. The major degradate, 3-chloropyridinol, was present in the water phase at a maximum of 18.0% of the applied at 4 months posttreatment, and was 11.8% at 2 months posttreatment. The major degradate, dichloropyridinol, was present in the water phase at a maximum of 44.0% of the applied at 2 weeks posttreatment, and decreased to 30.7% and 23.2% of the applied by 4 weeks and 2 months posttreatment, respectively. At 2 months posttreatment, unextracted [<sup>14</sup>C]residues comprised 38.3% of the applied and adiolabeled <sup>14</sup>CO<sub>2</sub> accounted for 11.4% of the applied. The data requirement (162-4) is satisfied. (MRID #44080345)

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## Soil Adsorption/Desorption (163-1)

The data requirement (163-1) is not satisfied because information on the mobility of the primary degradates of fluroxypyr acid, dichloropyridinol and methoxypyridine, is not acceptable at this time.

Based on batch equilibrium studies (MRID #42137319), fluroxypyr acid was determined to be very mobile in silt loam, sandy loam, loam and silty clay soil:solution slurries equilibrated for 16 hours at 21-24° C. The test soils were the identical 4 soils studied in the aerobic soil metabolism study discussed previously. The experimentally-determined Freundlich  $K_{ads}$  (ml/g) were 1.7 for the silt loam, 0.11 for the sandy loam; 1.9 for the loam, and 1.0 for the silty clay; respective  $K_{oc}$  values were 78, 51, 62 and 81. The acid dissociation constant (pKa =2.94) indicates fluroxypyr acid will occur predominantly as the anionic (i.e., negatively-charged) species under typical environmental conditions. Also, the solubility of fluroxypyr acid is pH-dependent ranging from 32 mg/L at pH 2.5 to 7.95 g/L at pH 7.5 (MRID #44080349). These characteristics further support the mobility interpretation for fluroxypyr acid.

Results of batch equilibrium studies with fluroxypyr-MHE (single point concentration of 0.066 mg/L) yielded K<sub>d</sub> values of 260 in a silt loam; 95 in sandy loam, 190 in loam and 210 in silty clay soil:solution slurries equilibrated for 10 minutes. The study authors used a 10-minute equilibration time due to the rapid transformation of fluroxypyr-MHE to fluroxypyr acid. It is unlikely that equilibrium was established during this experiment since the ester rapidly transforms to the acid. (MRID #42137319)

#### Soil Adsorption/Desorption of Degradates

The data requirement (163-1) is not satisfied. The submitted study (MRID #44094903) is not scientifically valid and does not provide useful information on the soil mobility (batch equilibrium) of the major fluroxypyr acid degradate [2,6-14C]dichloropyridinol (4-amino-3,5-dichloro-6-fluoro-2-pyridinol) in four soils or [2,6-14C]methoxypyridine (4-amino-3,5-dichloro-6-fluoro-2-methoxypyridine) in four foreign soils. In the dichloropyridinol and methoxypyridine studies, adsorption and desorption data were incomplete. Also, for the methoxypyridine study conducted according to OECD guidelines, (i) the four non-U.S. soils were not adequately compared with domestic (USA) soils; and (ii) at least one of the soils must have an organic matter content of less than 1%.

### Volatility - Lab and Field (163-2 and 163-3)

The reported vapor pressure for fluroxypyr-MHE is 1.07 E-7 mm Hg at 25° C. Using the vapor pressure of 1.07 E-7 mm Hg at 25° C, the estimated Henry's Law Constant  $(K_H)$  is 5.75 E-8 atm- $m^3$ /mol. The volatility data requirements (163-2: Laboratory Volatility; 163-3: Field Volatility) are waived based on the reported low vapor pressure and  $K_H$  which suggests volatilization would not be a significant route of dissipation.

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## Terrestrial Field Dissipation (164-1)

The data requirement (164-1) is not satisfied at this time. The storage stability study (MRID #44080355) does not meet Subdivision N Guidelines for the terrestrial field dissipation of fluroxypyr MHE and fluroxypyr (acid) because adequate storage stability data were not submitted for soils collected from the test sites. The soil used in the storage stability study was not representative of the soils found at the test sites, particularly in ND and WA. The terrestrial field dissipation study (MRID #44080347) may be upgraded with the submission of acceptable frozen storage stability data for fluroxypyr MHE, fluroxypyr (acid), and metabolites using soils obtained from the respective test sites.

Fluroxypyr residues were slightly persistent in terrestrial field dissipation studies conducted at three locations in the United States. Total fluroxypyr residues (fluroxypyr MHE plus fluroxypyr) dissipated in Putnam silty clay loam, Gardena sandy clay loam, and Quincy loamy sand soils in MO, ND, and WA, respectively, with registrant-calculated half-lives of 24.8, 36.3, and 13.2 days in plots vegetated with spring wheat (see Table AB). In the 0- to 6-inch soil depth, fluroxypyr MHE was present at maximum concentrations of 29 to 140 ng/g soil by 3 to 7 DAT; fluroxypyr (acid) was observed at maximum concentrations of 180 to 220 ng/g. The pyridinol metabolite was observed at a maximum concentration of 12 ng/g in ND, sporadically at <10 ng/g in WA, and was not detectable in MO. The methoxypyridine metabolite was observed at maximum concentrations of 25 to 50 ng/g at all three test sites.

Results from these terrestrial field studies and supporting laboratory information suggest fluroxypyr-MHE and fluroxypyr acid dissipated principally by hydrolysis and microbial-mediated metabolism. The rate of dissipation limited downward transport (i.e., leaching) in the submitted studies. The fluroxypyr-MHE and fluroxypyr acid were confined primarily to the 0- to 6-inch soil depth; no data were reported for analyses of the parent below the 6-inch depth at MO and WA. The fluroxypyr metabolites pyridinol and methoxypyridine were detected at all three test locations primarily in the 0- to 6-inch soil depth. Fluroxypyr MHE and its metabolites were not detected below the 6-inch depth, except for methoxypyridine in WA at two months after treatment (2 MAT), which was observed at <10 ng/g in the 6- to 12-inch and 12- to 18-inch soil depths. The subsoil permeability at the MO site was 0-0.06 in/hr from 17 to 34 inches depth for the Putnam silty clay loam. Total water input via irrigation and precipitation was 137, 135, and 153% of the 30-year historical precipitation average in MO, ND, and WA, respectively. Pan evaporation data were not reported for any site.

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Table AB. Soil Properties for Field Dissipation Studies

Site	Soil Series	Soil Classification	Minimum Permeability Range (in/hr)
Missouri	Putnam	fine, montmorillonitic, mesic Mollic Albaqualfs	0.0-0.06 at 17-34"
North Dakota	Gardena	coarse-silty, mixed Pachic Udic Haploborolls	0.6-2.0 at 0-60"
Washington	Quincy	mixed, mesic Xeric Torripsaments	6-20 at 0-60"

Detailed descriptions of the residue analytical methods ACR 91.10 and GRM 93.03 were not included in the terrestrial dissipation study (MRID 44080347), but were described in the accompanying storage stability study (MRID 44080355).

#### Bioaccumulation in Fish (165-4)

The data requirement (165-4) is not satisfied at this time. This submitted study (MRID #44080348) does not provide adequate information on the bioaccumulation of fluroxypyr-MHE or fluroxypyr acid in fish. Although the method validation study indicated that HPLC column recoveries of radioactivity from fish tissue extracts were adequate, column recoveries of radioactivity from fortified water samples were only 67% and 65% of the applied for samples analyzed at 30 minutes and 24 hours posttreatment, respectively. The reported aqueous concentration data represent adjusted values (to correct for parent compound loss presumed to have occurred during column injection); therefore, bioconcentration factors (BCF) based on the aqueous concentration of the parent compound are suspect. Additionally, the aqueous concentration of the parent compound was not constant, but varied from 0.168 to 0.42 ng/mL throughout the exposure period.

This study does not meet Subdivision N Guidelines for the fulfillment of EPA data requirements on bioaccumulation in fish for the following reasons: (1) rainbow trout were used to study the bioaccumulation of fluroxypyr MHE in a laboratory setting; the recommended species is either bluegill sunfish or channel catfish; (2) the analytical method was inappropriate and could not adequately recover the parent compound or its degradates from water samples; (3) the aqueous concentration of the pesticide (in the form of the parent compound) was not reasonably constant, but varied between 11% and 29% of the nominal application (based on values adjusted to correct for method inadequacies); and (4) complete tissue concentration data (for fluroxypyr-MHE and fluroxypyr acid) were not reported for each tissue type and sampling interval. The submitted study cannot be upgraded; a new study is required.

#### C. Water Resources Assessment

The Water Resources Assessment discusses the screening model results in both surface water and ground water media for fluroxypyr. Water resource monitoring data are not available for fluroxypyr-MHE and fluroxypyr acid or its degradates.

#### Surface Water Assessment

Data reported in Table XX presents the maximum acute and chronic surface water concentrations estimated from GENEEC Version 1.2 modeling. For surface water resources, the maximum acute estimated environmental concentration (EEC) was 11.2  $\mu$ g/L and the maximum chronic EEC was 3.9  $\mu$ g/L when fluroxypyr was modeled at 0.25 lbs acid equivalents/A/yr using aerial application. The modeling inputs are shown in Table YY.

Table XX. Surface Water EECs (µg/L) using GENEEC Version 1.2

Maximum EEC	Mean 4-Day EEC	Mean 21-Day EEC	Mean 56-Day EEC
11.2	10.4	7.1	3.9

In aquatic environments, fluroxypyr-MHE is rapidly hydrolyzed to fluroxypyr acid which has herbicidal activity. Fluroxypyr acid is further degraded (although less rapidly) via microbial-mediated metabolism to "pyridinol" and "methoxypyridine" degradates.

Table YY. Surface Water Exposure Assessment using GENEEC (V1.2)

MODEL INPUT VARIABLE	INPUT VALUE
Application Rate (lbs ai/A)	0.25
Maximum No. of Applications	1
Application Interval (appls./year)	Not applicable (single appl.)
Koc	50 (minimum reported value)
Aerobic Soil Metabolic Half-life (days)	23 (maximum of 4 reported values)
Is the pesticide wetted-in?	No
Depth of Incorporation (in.)	0.0
Spray Drift	Aerial (5%)
Solubility (mg/L)	0.90
Aerobic Aquatic Metabolic Half-life (days)	14

pH 7 Hydrolysis Half-life (days)	stable (454 days; extrapolated from a 30-day study)
Photolysis Half-life (days)	0 (stable )

In aerobic soil environments, fluroxypyr acid and the pyridinol and methoxypyridine degradates are ultimately metabolized to carbon dioxide (totaled 46.8-76.2% of the applied radioactivity in the aerobic soil metabolism study).

#### Groundwater Assessment

Results of the Groundwater Screening Assessment using SCI-GROW2 estimated the acute and chronic EECs for groundwater to be 0.025  $\mu$ g/L. Model input values for SCI-GROW2 are listed in Table ZZ.

Table ZZ. Ground Water Exposure Assessment using SCI-GROW2

MODEL INPUT VARIABLE	INPUT VALUE
Application Rate (lbs. ai/A)	0.25
Maximum No. of Applications	1
Koc	68 (median; n = 4)
Aerobic Soil Metabolic Half-life (days)	14 (mean; n = 4)

#### D. Environmental Chemistry Method Validation

The analytical method (GRM #93.03) for the determination of fluroxypyr acid and the degradates, methoxypyridine and pyridinol in soil was submitted to the Analytical Chemistry Branch, BEAD/OPP on 10/25/96. The review of this method is not currently available.

#### 2. Exposure Assessment

#### a. Terrestrial

For pesticides applied as a liquid product, the estimated environmental concentrations (EECs) on food items following product application are compared to LC<sub>50</sub> values to assess risk. Table 1 gives the predicted 0-day maximum and mean residues of a pesticide that may be expected to occur on selected avian or mammalian food items immediately following a direct single application at 1 lb ai/A.

tests with freshwater fish are not required for fluroxypyr acid or fluroxypyr MHE.

#### iii. Freshwater Invertebrates, Acute

A freshwater aquatic invertebrate toxicity test using the TGAI is required to establish the toxicity of fluroxypyr to aquatic invertebrates. The preferred test species is *Daphnia magna*. Results of this test are given in Table 8.

Table 8. Acute Toxicity to Freshwater Invertebrates

Species/Test Type	% ai	48-hour EC50 (mg ai/L)	Toxicity Category	MRID No. Author/Year	Study Classification
-		Fluro	хрут Acid		
Water flea (Daphnia magna)	99	>100	Practically nontoxic	402444524 Jones, 1984	Core .
		Flurox	урут МНЕ		
Water flea (Daphnia magna)	98.5	>0.11	Not determined <sup>1</sup>	42137308 Weinberg, Milazzo, Servinski, and Rick, 1991	Core
Water flea (Daphnia magna)	Not reported	>0.6	Not determined	40244520 Jones, 1984	Core

<sup>1</sup> Test concentrations up to the solubility limit caused no mortality.

Since the  $LC_{50's}$  for the water flea is greater than 100 ppm, fluroxypyr acid is considered practically nontoxic to freshwater invertebrates on an acute basis. Acute toxicity tests failed to determine  $LC_{50}$ 's for fluroxypyr MHE because motality did not occur when tested up to the solubility limit. Since fluroxypyr MHE is not acutely toxic at its solubility limit, it is also considered practically nontoxic to freshwater invertebrates on an acute basis.

#### iv. Freshwater Invertebrate, Chronic

Because of the low acute toxicity to *Daphnia magna*, freshwater invertebrate life-cycle tests are not required for fluroxypyr acid or fluroxypyr MHE. However, a study of the chronic toxicity of fluroxypyr MHE to *Daphnia magna* has been submitted (MRID 44080314; Kirk et al., 1996). The percent purity of the active ingredient was 95.8%. This was a 21 day flow through study with mean measured concentrations. The reported NOEC and LOEC were 60.5 mg ai/L and 109 mg ai/L, respectively, based on number of young produced per adult. This study was classified as supplemental because it was suspected that undissolved test material was present in the test solutions. The mean measured concentrations in this study were probably an overestimation of the actual exposure, which would have inflated the toxicity estimates.

#### c. Toxicity to Estuarine and Marine Animals

#### i. Estuarine and Marine Fish, Acute

Acute toxicity testing with estuarine/marine fish using the TGAI is required for fluroxypyr because the end-use product the active ingredient is expected to reach the marine/estuarine environment because of its use in coastal areas. The preferred test species is sheepshead minnow. Results of these tests are given in Table 9.

Table 9. Acute Toxicity Estuarine/Marine Fish

Species, Test Type	% ai	96-hour LC50 (mg ai/L)	Toxicity Category	MRID No. Author/Year	Study Classification
		Fluroxy	рут Acid		
Silverside ( <i>Menidia beryllina</i> ), Flow-through	98.7	40 (measured)	Slightly toxic	44080309 Boeri, Kowalski, and Ward, 1996	Core
		Fluroxy	ovr MHE		
Sheepshead minnow (Cyprinodon variegatus), Flow-through	95.8	>0.087 (measured)	Not determined	44080308 Boeri, Kowalski, and Ward, 1996	Core
Atlantic Silverside (Menidia menidia), Flow-through	99.1	>0.19 (measured)	Not determined <sup>2</sup>	42137309 Manning, 1988	Supplemental

<sup>1</sup> A test concentration at the solubility limit caused no mortality.

Since the  $LC_{50}$  for the silverside falls in the range of 10 to 100 ppm, fluroxypyr acid is considered slightly toxic to estuarine and marine fish on an acute basis. Acute toxicity tests failed to determine  $LC_{50}$ 's for fluroxypyr MHE because motality did not occur when tested up to the solubility limit. Since fluroxypyr MHE is not acutely toxic at its solubility limit, it is also considered practically nontoxic to estuarine and marine fish on an acute basis.

#### ii. Estuarine and Marine Fish, Chronic

Because of the low acute toxicity, early life-stage and fish life-cycle tests with estuarine/marine fish are not required for fluroxypyr acid or fluroxypyr MHE.

#### iii. Estuarine and Marine Invertebrates, Acute

Acute toxicity testing with estuarine/marine invertebrates using the TGAI is required for fluroxypyr because the end-use product is intended for direct application to the marine/estuarine environment or the active ingredient is expected to reach this environment because of its use in coastal counties. The preferred test species are mysid shrimp and eastern oyster. Results of these tests are given in Table 10.

<sup>2</sup> Test concentrations up to the solubility limit caused no mortality.

Table 10. Acute Toxicity to Estuarine/Marine Invertebrates

Species/Test Type	% ai.	96-hour LC <sub>so</sub> or EC50 (mg ai/L)	Toxicity Category	MRID No. Author/Year	Study Classification
· 		Fluroxy	рут Acid		
Eastern oyster				44080311	
(Crassostrea virginica),				Boeri, Kowalski, and	
Flow-through shell deposition	98.7	51 (measured)	Slightly toxic	Ward, 1994	Core
Grass shrimp				44080312	
(Palaemonetes pugio),				Boeri, Kowalski, and	
Flow-through	98.7	>120 (measured)	Practically nontoxic	Ward, 1994	Core
		Fluroxy	oyr MHE		
Eastern oyster				44080310	
(Crassostrea virginica),				Boeri, Kowalski, and	
Flow-through shell	95.8	0.068 (measured)	Very highly toxic	Ward, 1995	Core
deposition					
Grass shrimp				44080313	
(Palaemonetes pugio),			•	Boeri, Kowalski, and	
Flow-through	95.8	> 0.135 (measured)	Not determined	Ward, .1995	Core
Pink shrimp (Penaeus				42137311	
duorarum), Flow-through	99.1	>0.13 (measured)	Not determined <sup>2</sup>	Manning 1988	Supplemental
Eastern ovster			•	42137310	Invalid

I A test concentrations at the solubility limit caused no mortality

Oysters appear to be more sensitive than shrimp and fish to fluroxypyr acid fluroxypyr MHE. Since the  $LC_{50}$  for the eastern oyster fall in the range of 10 to 100 ppm, fluroxypyr acid is considered slightly toxic to estuarine and marine invertebrates on an acute basis. Fluroxypyr MHE had an  $LC_{50}$  of only 68 ppb, categorizing it as very highly toxic to estuarine and marine invertebrates on an acute basis. Fluroxypyr MHE is not toxic to shrimp at its solubility limit.

#### iv. Estuarine and Marine Invertebrate, Chronic

A life-cycle tests with a estuarine/marine invertebrate are not required for fluroxypyr acid or fluroxypyr MHE. Fluroxypyr MHE has high acute toxic to marine/estuarine mollusks, but is predicted to rapidly degrade to the much less toxic fluroxypyr acid in saltwater. Furthermore, both fluroxypyr MHE and fluroxypyr acid have been shown to have low toxicity to marine/estuarine crustaceans.

#### d. Toxicity to Plants

#### i. Terrestrial

Terrestrial plant testing is required for fluroxypyr because it is an herbicide that has terrestrial non-residential outdoor use patterns, may move off the application site by drift from

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<sup>2</sup> Five percent mortality occurred at the solubility limit.

chemigation, and may have endangered or threatened plant species associated with the application sites. The required testing consists of seedling emergence and vegetative vigor tests with ten crop species. Six of the species must be dicotyledonous and represent at least four families. One of these species must be soybean (Glycine max) and a second must be a root crop. The remaining four species must be monocotyledonous and represent at least two families. One of these species must be corn (Zea mays). Tier 1 tests (GLN 122-1) may be conducted to measure the response of plants, relative to a control, at a test level that is equal to the highest use rate (expressed as lbs ai/A) or three times the EEC for nontarget areas. Tier 2 tests (GLN 123-1) are required for any test species that shows a reduction in response equal to or greater than 25% in the tier 1 tests.

Results of Tier II seedling emergence toxicity testing with a formulated product of fluroxypyr MHE are given in Table 11. Monocots appear to be more sensitive to effects on seedling emergence than dicots. The most sensitive species was cucumber. Based on the most sensitive parameter, phytotoxic symptoms, 25% inhibition was predicted to occure at a dose of 0.075 lb ai/A. The no observed effect level (NOEL) was 0.031 lb ai/A. The guideline requirement for seedling emergence testing [123-1(a)] is fulfilled for all test species.

Table 11. Phytotoxicity of Fluroxypyr MHE--Tier II Seedling Emergence Tests

Species	% Al	Most Sensitive Parameter	EC <sub>25</sub> (lb ai/A)	NOEC (lb ai/A)	MRID No. Author/Year	Study Classification
Corn (monocot)	26.9	All similar	>0.25	0.25	44080335	Core
Onion (monocot)		All similar	>0.25	0.25	Schwab, 1996	Core
Ryegrass (monocot)		Phytotoxic symptoms	>0.25	0.124		Core
Wheat (monocol)		All similar	> 0.25	0.25		Core
Cotton (dicót)		Phytotoxic symptoms	0.125	0.062		Core
Cucumber (dicot)		Phytotoxic symptoms	0.075	0.031		Core
Radish (dicot)		All similar	>0.25	0.25		Core
Soybean (dicot)		Phytotoxic symptoms	0.24	0.062		Core
Sunflower (dicot)		Phytotoxic symptoms	0.109	0.062		Core
Tomato (dicot)		Shoot fresh	0.142	0.124		Core

<sup>1</sup> This NOEL is based on 17% mortality of plants occurring at the next higher test level, 0.011 lb ai/A.

The most sensitive test species for seedling emergence effects was cucumber. The  $EC_{25}$  and the NOEC for cucumber are 0.075 and 0.031 lb ai/A. Fluroxypyr MHE is generally not

<sup>2</sup> Seedling emergence data for ryegrass is upgraded from supplemental to core.

toxic to monocots at 0.25 lb ai/A.

Results of Tier II seedling vegetative vigor toxicity testing on a formulated product of fluroxypyr MHE are given in Table 12. Monocots appear to be more sensitive than dicots to effects on vegetative vigor. The most sensitive species was cotton. Based on the most sensitive parameter, phytotoxic symptoms, 25% inhibition was predicted to occure at a dose of 0.0012 lb ai/A. The no observed effect level (NOEL) was 0.0010 lb ai/A.

Table 12. Phytotoxicity of Fluroxypyr MHE--Tier II Vegetative Vigor Tests

Species	% AI	Most Sensitive Parameter	EC <sub>25</sub> (lb ai/A)	NOEC (lb ai/A)	MRID No.; Author/Year	Study Classification
Corn (monocot)	26.9	Phytotoxic symptoms	0.176	0.031	44080335; Schwab, 1996	Core
Onion (monocot)		Phytotoxic symptoms	0.124	0.062		Core
Ryegrass (monocot)		All similar	>0.25	0.25		Core
Wheat (monocot)		Phytotoxic symptoms	>0.25	0.062		Core
Cotton (dicot)		Phytotoxic symptoms	0.0012	0.0010		Core
Cucumber (dicot)		Phytotoxic symptoms	0.010	0.004		Core `
Radish (dicot)		All similar	0.056	0.031		Core
Soybean (dicot)		Phytotoxic symptoms	0.008	0.004		Core
Sunflower (dicot)		Phytotoxic symptoms	0.004	0.001	·	Core
Tomato (dicot)		Shoot fresh weight	0.004	0.001		Core

Vegetative vigor effects occur at lower levels than do seedling emergence effects. The most sensitive test species for vegetative vigor effects was cotton, for which the  $EC_{25}$  and NOEC were 0.0012 and 0.0010 lb ai/A, respectively. Fluroxypyr MHE is much less toxic to monocots.

The registrant has provided additional data from a non-GLP study that provide information on the phytotoxicity of three degradation products of fluroxypyr MHE: fluroxypyr acid, methoxypyridine, and pyridinol (MRID 44094902). The data provided by this study for effects on nontarget terrestrial plants are invalid for the tier II test guideline (GLN 122-1), meaning that the EC<sub>25</sub> values generated cannot be used in this risk assessment. However, the data were classified as supplemental for the tier I test guideline (GLN 122-1), meaning that they do not fulfill the guideline requirement but do provide some useful information. The study demonstrates that the degradation products have little or no phytotoxicity activity. For

both seedling emergence and vegetative vigor effects, these degradation product caused less than 25% inhibition when tested at 0.5 lb ai/A in the following crops: cotton, radish, soybean, sunflower, corn, and wheat. No additional testing of methoxypyridine and pyridinol are required with these species. However, tier I or tier II seedling emergence and vegetative vigor data are still needed for two additional species of monocots, representing two different families, and two additional species of dicots representing two different families (memo from Michael Davy to Joanne Miller, 1/22/98, D239606).

The phytotoxicity study decribed above also shows that the phytotoxicity of fluroxypyr acid is greater than that of the parent compound, fluroxypyr MHE. For seedling emergence effects, fluroxypyr acid caused less than 25% inhibition to corn and radish when tested at 0.5 lb ai/A. Seedling emergence testing with fluroxypyr acid is not required for these two species. but is required for three other species of monocots, representing two families, and five other species of dicots (memo from Michael Davy to Joanne Miller, 1/22/98, D239606). For vegetative vigor effects, fluroxypyr acid caused less than 25% inhibition to corn, wheat, sunflower, and radish when tested at 0.5 lb ai/A. Vegetative vigor testing with fluroxypyr acid is not required for these four species, but is required for two additional species of monocots, representing two families, and four additional species of dicots (memo from Michael Davy to Joanne Miller, 1/22/98, D239606). For all of these tests, tier I tests are required, but tier II tests may be provided in lieu of tier I tests.

Since fluroxypyr MHE might degrade to fluroxypyr acid before reaching nontarget plants, data on the phytotocicity of fluroxypyr acid to emerging seedlings is given in Table 13.

T-1-12	Phytotoxicity of Fluroxypyr	Anial Tion II	Candling	Emargana Tosta
Table 13.	Phytotoxicity of Filiroxypyr	Acid Her II	Seediing	Emergence lesis

Species	% AI	Most Sensitive Parameter	EC <sub>23</sub> (Ib ai/A)	MRID No.; Author/Year	Study Classification
Corn (monocot)	99.6	Fresh weight	0.178	44094902; Wright nd Rowland, 1996	Supplemental
Wheat (monocot)		Fresh weight	0.079	Rowland, 1990	Supplemental
Cotton (dicot)		Fresh weight	0.025		Supplemental
Radish (dicot)		Fresh weight	0.295		Supplemental
Soybean (dicot)		Fresh weight	0.072		Supplemental
Sunflower (dicot)		Plant height	0.036		Supplemental

Based on supplemental data, fluroxypyr acid is more toxic to emerging seedlings than fluroxypyr MHE. The most sensitive of the six species tested is cotton, which has an  $EC_{25}$  of 0.025 lb ai/A. This is approximately 5 times lower than the cotton  $EC_{25}$  for fluroxypyr MHE.

#### ii. Aquatic Plants

Aquatic plant testing is required for fluroxypyr because it is an herbicide that has outdoor

non-residential terrestrial uses that may move off-site in spray drift from aerial applications. The following species should be tested at tier 2: Kirchneria subcapitata, Lemna gibba, Skeletonema costatum, Anabaena flos-aquae, and a freshwater diatom. Results of tier 2 toxicity testing with fluroxypyr are given in Table 14.

Table 14. Nontarget Aquatic Plant Toxicity (Tier 2)

Species	% AI	EC∞ (ppm)	NOEC (ppm)	MRID No. Author/Year	Study Classification
<del></del>		Fluro	хурут Acid		
Green algae Kirchneria subcapitata	99.2	<del>-</del>		42164501 Cowgill, Milazzo, and Murphy, 1988	Invalid
Green algae chlorella vulgaris	99	>100	100	40244526 Jones, 1984	Supplemental/I
<del></del>		Fluro	сурут МНЕ	·	
Green algae Kirchneria subcapitata	98.5	>1.6	0.12	42137312 Hughes and Alexander, 1991	Supplemental/2
Green algae Kirchneria subcapitata	95.8	>1.4	0.20	44080340 Milazzo, Hugo, and Martin. 1996	Core
Duckweed <i>Lemna gibba</i>	95.8	>2.3	1.2	44080338 Milazzo, Hugo, and Martin, 1996	Core
Blue-green Algae Anabaena flos-aquae	95.8	0.40	U.030	44080336 Milazzo, Hugo, and Martin. 1996	Core
Marine diatom Skeletonema costatum	95.8	0.29	0.18	44080337 Milazzo, Hugo, and Martin. 1996	Core
Freshwater Diatom Navicula pelliculosa	<del></del>			44080339 Milazzo, Hugo, and Martin. 1996	Invalid
4-amino-3,5-dichloro-6-fluro-2-m	ethoxypyridine				
Green algae Kirchneria subcapitata	99.9	2.4	0.94	44080341 Kirk and Landre, 1995	Supplemental/3

<sup>1</sup> The test species is not an acceptable in US guidelines, and cell counts were not determined.

No acceptable aquatic plant toxicity data are available for fluroxypyr acid. Supplemental data, however, indicate that it has low toxicity to green algae. Additional data are not required on the fluroxypyr acid for registration of products containing fluroxypyr MHE.

Data on the toxicity of fluroxypyr MHE to aquatic plants are complete with the exception of data for a freshwater diatom, such as *Navicula pelliculosa*. A new study with a freshwater diatom is required. The test guideline for tier II aquatic plant testing (123-2) is not fulfilled.

<sup>2</sup> Because of lack of solubility, the concentration of test material in solution during the test was uncertain.

<sup>3.</sup> This study did not comply with GLP standards .

The study with 4-amino-3,5-dichloro-6-fluro-2-methoxypyridine (MRID 44080341) is not a GLP study, but it provides usable information on the toxicity of this degradation product of fluroxypyr.

#### 3. Exposure and Risk Characterization

Risk characterization integrates the results of the exposure and ecotoxicity data to evaluate the likelihood of adverse ecological effects. The means of this integration is called the quotient method. For this method, risk quotients (RQs) are calculated by dividing exposure estimates by acute and chronic ecotoxicity values:

#### RQ = EXPOSURE/TOXICITY

RQs are then compared to OPP's levels of concern (LOCs). These LOCs are criteria used by OPP to indicate potential risk to nontarget organisms and the need to consider regulatory action. The criteria indicate that a pesticide used as directed has the potential to cause adverse effects on nontarget organisms. LOCs currently address the following risk presumption categories: (1) acute high--potential for acute risk is high; regulatory action may be warranted in addition to restricted use classification, (2) acute restricted use--the potential for acute risk is high but may be mitigated through restricted use classification, (3) acute endangered species-endangered species may be adversely affected; regulatory action may be warranted, and (4) chronic risk--the potential for chronic risk is high; regulatory action may be warranted. Currently, EFED does not perform assessments for chronic risk to plants, acute or chronic risks to nontarget insects, or chronic risk from granular/bait formulations to birds or mammals.

The ecotoxicity test values (i.e., measurement endpoints) used in the acute and chronic risk quotients are derived from required studies. Examples of ecotoxicity values derived from short-term laboratory studies that assess acute effects are: (1) LC50 (fish and birds). (2) LD50 (birds and mammals), (3) EC50 (aquatic plants and aquatic invertebrates), and (4) EC25 (terrestrial plants). Examples of toxicity test effect levels derived from the results of long-term laboratory studies that assess chronic effects are: (1) LOEC (birds, fish, and aquatic invertebrates), (2) NOEC (birds, fish and aquatic invertebrates), and (3) MATC (fish and aquatic invertebrates). For birds and mammals, the NOEC is generally used as the ecotoxicity test value in assessing chronic effects, although other values may be used when justified. Generally, the MATC (defined as the geometric mean of the NOEC and LOEC) is used as the ecotoxicity test value in assessing chronic effects to fish and aquatic invertebrates. However, the NOEC is used if the measurement end point is production of offspring or survival.

Risk presumptions, along with the corresponding RQs and LOCs, are tabulated below.

Risk Presumptions for Terrestrial Animals

Risk Presumption	RQ	LOC
Acute High Risk	EEC1/LC50 or LD50/sqft2 or LD50/day1	0.5
Acute Restricted Use	EEC/LC50 or LD50/sqft or LD50/day (or LD50 < 50 mg/kg)	0.2
Acute Endangered Species	EEC/LC50 or LD50/sqft or LD50/day	0.1
Chronic Risk	EEC/NOEC	1

<sup>&</sup>lt;sup>1</sup> abbreviation for Estimated Environmental Concentration (ppm) on avian/mammalian food items

LD50 \* wt. of bird

Risk Presumptions for Aquatic Animals

Risk Presumption	RQ	LOC
Acute High Risk	EEC1/LC50 or EC50	0.5
Acute Restricted Use	EEC/LC50 or EC50	0.1
Acute Endangered Species	EEC/LC50 or EC50	0.05
Chronic Risk	EEC/MATC or NOEC	ı

<sup>1</sup> EEC = (ppm or ppb) in water

Risk	Presump	otions	for	Plants
ACI3E	I I Count	LIUIIS	101	Liants

Risk Presumption	RQ	LOC
	Terrestrial and Semi-Aquatic Plants	
Acute High Risk	EEC¹/EC25	!
Acute Endangered Species	EEC/EC05 or NOEC	ì
	Aquatic Plants	
Acute High Risk	EEC <sup>2</sup> /EC50	1
Acute Endangered Species	EEC/EC05 or NOEC	

<sup>&</sup>lt;sup>1</sup> EEC = lbs ai/A

# a. Risk to Nontarget Terrestrial Animals

#### i. Birds

In subacute toxicity tests, fluroxypyr acid and fluroxypyr MHE caused no mortality of mallards and northern bobwhites at the highest test concentrations. The highest test concentrations were 5620 ppm and 5000 ppm in tests with the mallard and the bobwhite.

<sup>&</sup>lt;sup>2</sup> mg/ft<sup>2</sup> mg.of.toxicant.consumed/day LD50 \* wt. of bird

<sup>&</sup>lt;sup>2</sup> EEC = (ppb/ppm) in water

respectively. Environmental concentrations of fluroxypyr in wildlife food items are not expected to approach these maximum test concentrations. The greatest EEC is only 60 ppm for application on short grass at 0.25 lb ai/A. Therefore, use of fluroxypyr is predicted to pose negligible risk to birds, including threatened and endangered species, based on acute effects.

Table 15 gives the chronic risk quotients for spray applications of fluroxypyr MHE. As a worst-case screen, chronic risk quotients were calculated based on day-0 EECs.

Table 15. Avian Chronic Risk Quotients for Single Application of EC Products Based on Maximum EECs and a NOEC of the Mallard.

Site. Appl. Method	Application Rate (lbs ai/A)	Food Items	Maximum EEC (ppm)	NOEC (ppm)	Chronic RQ (EEC/NOEC)
Wheat, Barley, and	0.125	Short grass	30	250	0.12
Oats		Tall grass	. 14	250	0.06
		Broadleaf plants and Insects	17	250	0.07
		Seeds	2	250	0.01
Uncultivated areas	0.25	Short grass	60	250	0.24
and Volunteer Potato Control in		Tall grass	28	250	0.11
Wheat, Barley, and Oats		Broadleaf plants and Insects	34	250	0.14
		Sceds	4	250	0.02

<sup>\*</sup> Exceeds chronic risk LOCs.

These risk quotients are based on day-0 EECs, which are likely greater than the chronic level of exposure to birds in the wild. This screen showed that no chronic risk quotient exceeds the avian acute level of concern of 1.0. Therefore, the Agency predicts that all uses of fluroxypyr MHE would pose minimal chronic risk to birds.

#### ii. Mammals

Estimating the potential for adverse effects to wild mammals is based upon EEB's draft 1995 SOP of mammalian risk assessments and methods used by Hoerger and Kenaga (1972) as modified by Fletcher *et al.* (1994). The concentration of fluroxypyr in the diet that is expected to be acutely lethal to 50% of the test population (LC<sub>50</sub>) is determined by dividing the LD<sub>50</sub> value (usually rat LD<sub>50</sub>) by the fraction of the body weight consumed per day. A risk quotient is then determined by dividing the EEC by the derived LC<sub>50</sub> value. Risk quotients are calculated for three separate weight classes of mammals (15, 35, and 1000 g), each presumed to consume four different kinds of food (grass, forage, insects, and seeds). The acute risk quotients for broadcast applications of EC products are given in Table 16.

Table 16.a. Acute Risk Quotients for Herbivorous and Insectivorous Mammals, Based on a Single Application of EC

Fluroxypyr Product

Application Body		% Body Rat			EEC (ppm)			Acute RQ'		
Rate (lbs ai/A)	Weight (g)	Weight Consumed	tht LD50		Forage & Small Insects	Large Insects	Short Grass	Forage & Small Insects	Large Insects	
<del>_</del>				Wheat, Bari	ley, and Oats				·	
0.125	15	95	880	30.0	16.9	1.88	0.03	0.02	<0.01	
0.125	35	66	880	30.0	16.9	1.88	0.02	0.01	< 0.01	
0.125	1000	15	880	30.0	16.9	1.88	0.01	<0.01	<0.01	
<u> </u>		Uncultivated	areas and Vo	lunteer Pota	to Control in V	Vheat, Barley,	and Oats			
0.25	15	95	880	60.0	33.8	3.75	0.07	0.04	<0.01	
0.25	35	66	880	60.0	33.8	3.75	0.05	0.03	0.01	
0.25	1000	15	880	60.0	33.8	3.75	0.01	0.01	:0.01	

RQ = EEC (ppm)

LD50 (mg/kg)/ % Body Weight Consumed

Table 16.b. Acute Risk Quotients for Graminivorous Mammals for a Single Application of EC Fluroxypyr Product

Application Rate (lb ai/A)	Body Weight (g)	% Body Weight Consumed	Rat LD50 (mg/kg)	EEC (ppm) Seeds	Acute RQ' Seeds
		Whe	at, Barley, and Oats		<u> </u>
0.125	15	21	880	1.88	0.01
0.125	35	15	880	1.88	~ 0.01
0.125	1000	3	880	1.88	< 0.01
	Unc	ultivated Areas and Volunt	eer Potato Control in When	at, Barley, and Oats	
0.25	. 15	21	880	3.75	- 0.01
0.25	35	15	880	3.75	0.01
0.25	1000	3	880	3.75	. 0.01

<sup>1</sup> RQ = <u>EEC (ppm)</u>

LD50 (mg/kg)/ % Body Weight Consumed

Risk quotients do not exceeds the LOC for high risk, restricted use classification, or risk to endangered species. Therefore, these uses of fluroxypyr MHE pose minimal acute risk

<sup>\*\*\*</sup> Exceeds acute high, acute restricted, and acute endangered species LOCs.

<sup>\*\*</sup> Exceeds acute restricted and acute endangered species LOCs.

<sup>\*</sup> Exceeds acute endangered species LOC.

<sup>\*\*\*</sup> Exceeds acute high, acute restricted, and acute endangered species LOCs.

<sup>\*\*</sup> Exceeds acute restricted and acute endangered species LOCs.

<sup>\*</sup> Exceeds acute endangered species LOC.

to mammals, including threatened and endangered species.

Table 17 gives the chronic risk quotients for broadcast applications of nongranular products.

Table 17. Mammalian Chronic Risk Quotients for Single Application of EC Products Based on Maximum EECs and a Reproductive NOEC of the Rat.

Site Appl Method	Application Rate (lbs ai/A)	Food Items	Maximum EEC (ppm)	NOEC (ppm)	Chronic RQ (EEC/NOEC)
Wheat, Barley, and	0.125	Short grass	30.0	2000	0.02
Oats		Tall grass	13.8 .	2000	0.01
		Broadleaf plants and Insects	16.9	2000	0.01
		Seeds	1.9	2000	<0.01
Uncultivated Areas and Volunteer	0.25	Short grass	60.0	2000	0.03
Potato Control in Wheat, Barley, and		Tall grass	27.5	2000	0.01
Oats		Broadleaf plants and Insects	33.8	2000	0.02
		Seeds	4	2000	< 0.01

<sup>\*</sup> Exceeds chronic risk LOCs.

None of the risk quotients exceed the chronic LOC of 1.0. Therefore, these uses of fluroxypyr MHE pose minimal acute risk to mammals, including threatened and endangered species.

#### iii. Insects

Currently, EFED does not assess risk to nontarget insects. However, because fluroxypyr MHE and fluroxypyr acid are practically nontoxic to honeybees, and because the use rates are relatively low, use of this herbicide is expected to pose minimal risk to bees and other beneficial insects.

#### b. Exposure and Risk to Nontarget Freshwater Animals

Environmental fate information indicates that fluroxypyr MHE will rapidly transform into fluroxypyr acid in natural waters. Exposure to aquatic organisms was therefore assessed based on the toxicity of and exposure to fluroxypyr acid.

#### i. Freshwater Fish

Table 18 gives risk quotients for freshwater fish.

Table 18. Freshwater Fish Acute Risk Quotients for Single Application Based on a Bluegill Sunfish LC to

Use Site	Application Method	Rate in lb ai/A	Number of Applications	LC50 (ppm)	Peak EEC (ppm)	Acute RQ (EFC/LC50)
Wheat, Barley, and	Unincorporated ground spray	0.125	1	14.3	0.0056	<0.01
Oats	Aerial spray	0.125	<u> </u>	14.3	0.0056	<0.01
Uncultivated Areas	Unincorporated ground spray	0.25	1	14.3	0.011	<0.01
Control in Wheat, Barley, and Oats	Aerial spray	0.25	1	14.3	0.011	<0.01

<sup>\*\*\*</sup> Exceeds acute high, acute restricted, and acute endangered species LOCs.

Risk quotients do not exceeds the LOC for high risk, restricted use classification, or risk to endangered species. Therefore, these uses of fluroxypyr MHE pose minimal acute risk to freshwater fish, including threatened and endangered species.

#### ii. Freshwater Invertebrates

Table 19 gives the acute risk quotients for freshwater invertebrates.

Table 19. Freshwater Invertebrate Acute Risk Quotients for Single Application Based on a Waterflea LC in

Use Site	Application Method	Rate in lb ai/A	Number of Applications	LC50 (ppm)	Peak EEC (ppm)	Acute RQ (EEC/LC50)
Wheat, Barley, and	Unincorporated ground spray	0.125	I	<i>~</i> 100	0.0056	0.01
Oats	Aerial spray	0.125	1	>100_	0.0056	< 0.01
Uncultivated Areas and Volunteer	Unincorporated ground spray	0.25	1	-100	0 011	0.01
Potato Control in Wheat, Barley, and Oats	Aerial spray	0.25	1	÷100	0.011	0.01

<sup>\*\*\*</sup> Exceeds acute high, acute restricted, and acute endangered species LOCs.

Acute risk quotients do not exceeds the LOC for high risk, restricted use classification, or risk to endangered species. Therefore, these uses of fluroxypyr MHE pose minimal acute risk to freshwater invertebrates, including threatened and endangered species.

Pyridinol is a degradation product of fluroxypyr acid. The 96-hr LC<sub>50</sub> of pyridinol for juveniles of six salmonid species ranged from 1.5 to 2.7 mg/L Wan et al. (1987). These values are over two orders of magnitude greater than the EEC for fluroxypyr acid. Since the EECs for pyridinol would be even less than those for fluroxypyr acid, production of pyridinol clearly poses minimal risk to freshwater fish.

<sup>\*\*</sup> Exceeds acute restricted and acute endangered species LOCs.

Exceeds acute endangered species LOC.

<sup>\*\*</sup> Exceeds acute restricted and acute endangered species LOCs.

<sup>\*</sup> Exceeds acute endangered species LOC.

Only supplemental data are available on the chronic toxicity of fluroxypyr MHE to freshwater invertebrates. Table 20 gives the **chronic** risk quotients for freshwater invertebrates.

Table 20. Freshwater Invertebrate Acute Risk Quotients for Single Application Based on a Waterflea LC<sub>xn</sub>

Use Site	Application Method	Rate (lb ai/A)	Number of Applications	NOEC (ppm)	21- Day Average EEC (ppm)	Acute RQ (EEC/LC50)
Wheat, Barley, and	Unincorporated ground spray	0.125	1	60.5	3.54	0.06
Oats	Aerial spray	0.125	11	60.5	3.56	0.06
Uncultivated Areas and Volunteer	Unincorporated ground spray	0.25	1	60.5	7.08	0.12
Potato Control in Wheat, Barley, and Oats	Aerial spray	0.25	1	60.5	7.12	0.12

Based on supplemental data, chronic risk quotients do not exceeds the LOC for high risk, restricted use classification, or risk to endangered species. Therefore, these uses of fluroxypyr MHE pose minimal chronic risk to freshwater invertebrates, including threatened and endangered species.

#### c. Estuarine and Marine Animals

Table 21 gives the acute risk quotients for estuarine and marine fish, and Table 22 gives the acute risk quotients for estuarine and marine invertebrates.

Table 21. Acute Risk Quotients for Estuarine and Marine Fish Based on a Sheepshead Minnow LC<sub>so</sub>

Use Site	Application Method	Rate in Ib ai/A	Number of Applications	LC50 (ppm)	Peak EEC (ppm)	Acute RQ (EEC/LC50)
Wheat, Barley, and	Unincorporated ground spray	0.125	1	40	0.0056	< 0.01
Oats	Aerial spray	0,125	11	40	0,0056	< 0.01
Uncultivated Areas and Volunteer	Unincorporated ground spray	0.25	1	40	0.011	< 0.01
Potato Control in Wheat, Barley, and Oats	Aerial spray	0.25	1	40	0.011	< 0.01

<sup>\*\*\*</sup> Exceeds acute high, acute restricted, and acute endangered species LOCs.

Risk quotients do not exceeds the LOC for high risk, restricted use classification, or risk to endangered species. Therefore, these uses of fluroxypyr MHE pose minimal acute risk to marine or estuarine fish, including threatened and endangered species.

<sup>\*\*</sup> Exceeds acute restricted and acute endangered species LOCs.

<sup>\*</sup> Exceeds acute endangered species LOC.

Use Site	Application Method	Rate in lb ai/A	Number of Applications	LC <sub>so</sub>	Peak EEC	Acute RQ (EEC/LC50)	
Wheat, Barley, and Oats	Unincorporated ground spray	0.125	1	51	0.0056	< 0.01	
	Aerial spray	0.125	1	51	0.0056	< 0.01	
Uncultivated Areas and Volunteer	Unincorporated ground spray	0.25	1	51	0.011	< 0.01	
Potato Control in Wheat, Barley, and	Aerial spray	0.25	1	51	0.011	< 0.01	

Table 22. Acute Risk Quotients for Estuarine and Marine Invertebrates Based on an Oyster LCs

Risk quotients do not exceeds the LOC for high risk, restricted use classification, or risk to endangered species. Therefore, these uses of fluroxypyr MHE pose minimal acute risk to freshwater fish, including threatened and endangered species.

#### d. Exposure and Risk to Nontarget Plants

### i. Plants in Terrestrial and Semiaquatic Habitats

The EFED does separate risk assessments for two categories of nontarget plants, terrestrial and semi-aquatic. Non-target terrestrial plants inhabit non-aquatic areas which are generally well drained. Non-target semi-aquatic plants inhabit low-lying areas that are usually wet, although they may be dry during certain times of the year. Both the terrestrial and semi-aquatic plants are exposed to pesticides from runoff, drift, and volatilization. They differ, however, in that terrestrial plants are assumed to be subjected to sheet runoff, whereas semi-aquatic plants are assumed to be subjected to channelized runoff.

The EFED assumes that runoff and spray drift will expose nontarget plants to a fixed percentage of the application rate. This percentage of runoff is normally assumed to be between 1% 2%, or 5%, depending on the mobility and water solubility of the active ingredient. Since fluroxypyr MHE rapidly degrades to fluroxypyr acid in natural water, fluroxypyr acid is considered the active ingredient in this assessment. Fluroxypyr acid is very mobile in soil and is very soluable in water. The percent runoff is therefore assumed to be 5%. Spray drift exposure is assumed to be 1% and 5% of the application rate for ground and aerial applications, respectively.

For non-target terrestrial plants, EFED assumes a scenario in which plants are exposed from sheet runoff. A treated site of 1 acre is assumed to drain into an adjacent area of 1 acre where terrestrial plants may be impacted. In the scenario used for non-target semi-aquatic plants, exposure from runoff is assumed to be from channelized runoff. A treated site of 10 acres is assumed to drain into a distant low-lying area of 1 acre where semi-aquatic plants may

<sup>\*\*\*</sup> Exceeds acute high, acute restricted, and acute endangered species LOCs.

<sup>\*\*</sup> Exceeds acute restricted and acute endangered species LOCs.

<sup>\*</sup> Exceeds acute endangered species LOC.

be impacted. Estimated environmental concentrations for terrestrial and semi-aquatic plants are given in Table 23. Formulae for calculating these EECs given in Appendix A.

Table 23: Estimated Environmental Concentrations (EECs) For Terrestrial and Semi-Aquatic Plants

Use Site, Application Method		Runoff Value	Runoff Loading			Total Loading		
	Use Rate (lb ai/A)		Sheet Runoff (lb ai/A)	Channelized Runoff (lb ai/A)	Spray Drift Loading (lb ai/A)	Adjacent Area (Sheet Runoff + Drift)	Semi-aquatic Area (Channel Run-off + Drift)	
Wheat, Barley, and								
Oats Ground	0.125	0.05	0.00625	0.0625	0.00125	0.0075	0.06375	
Aerial	0.125	0.05	0.00375	0.0375	0.00625	_0.01	0.04375	
Uncultivated Areas and Volunteer Potato Control in Wheat. Barley, and Oats								

Risk to emerging seedlings was assessed by comparing the EECs listed above with levels in the seedling emergence study that caused 25% mortality most sensitive test species. The seedling emergence  $EC_{25}$  for the most sensitive species, cucumber, is 0.075 lb ai/A. Table 24 gives the risk quotients for emerging seedlings.

Table 24. Exposure and Risk Quotients for Seedling Emergence Effects of Fluroxypyr MHE on Terrestrial and Semi-aquatic Plants, Based on a Cucumber EC<sub>15</sub> of 0.075 lb ai/A

Use site	Application Method	Type of Plants	Exposure Scenario	EEC (lb ai/A)	Risk Quotients
Wheat, Barley,	Ground Spray	Terrestrial	Sheet runoff + spray drift	0.0075	0.10
		Semi-aquatic	Channelized runoff + spray drift (1%)	0.064	0.85
Wheat, Barley, and Oats	Aerial Spray	Terrestrial	Sheet runoff + spray drift (5%)	0.010	0.13
	·	Semi-aquatic	Channelized runoff + spray drift (5%)	0.044	
Uncultivated Areas and Volunteer Potato	Ground Spray	Terrestrial	Sheet runoff + spray drift (1%)	0.015	0.20
Control in Wheat, Barley, and Oats		Semi-aquatic	Channelized runoff + spray drift (1%)	0.13	1.7
Uncultivated Areas and Volunteer Potato	Aerial Spray	Terrestrial	Sheet runoff + spray drift (5%)	0.020	0.27
Control in Wheat, Barley, and Oats		Semi-aquatic	Channelized runoff + spray drift (5%)	0.088	1.2

The risk quotients indicate that use of fluroxypyr MHE at 0.25 lb ai/A would pose risk to nontarget plants in semiaquatic areas through effects on seedling emergence. However, these risk quotients only slightly exceed the high risk LOC, indicating that this risk is only marginal. Use on wheat, barley, and oats at 0.125 lb ai/A poses negligible risk to nontarget plants through effects on seedling emergence.

Risk to emerging seedlings also was assessed based on the phytotoxicity of fluroxypyr acid. Since fluroxypyr MHE rapidly degrades to fluroxypyr acid through base-catalyzed hydrolysis and microbial-mediated metabolism, nontarget plants could be exposed to runoff containing fluroxypyr acid. The seedling emergence  $EC_{25}$  for the most sensitive species, cotton, is 0.025 lb ai/A. Table 25 gives the risk quotients for emerging seedlings.

Table 25. Exposure and Risk Quotients for Seedling Emergence Effects of Fluroxypyr Acid on Terrestrial and Semi-aquatic Plants, Based on a Cotton EC<sub>35</sub> of 0.025 lb ai/A

Use site	Application Method	Type of Plants	Exposure Scenario	EEC (lb ai/A)	Risk Quotients
Wheat, Barley, and Oats	Ground Spray	Terrestrial	Sheet runoff +spray drift (1%)	0.0075	0.30
		Semi-aquatic	Channelized runoff + spray drift (1%)	0.064	2.6
Wheat, Barley, and Oats	Aerial Spray	Terrestrial	Sheet runoff + spray drift (5 %)	0.010	0.04
		Semi-aquatic	Channelized runoff + spray drift (5%)	0.044	1.8
Uncultivated Areas and Volunteer Potato	Ground Spray	Terrestrial	Sheet runoff $+$ spray drift (1%)	0.015	0.60
Control in Wheat, Barley, and Oats		Semi-aquatic	Channelized runoff + spray drift (1%)	0.13	5.2
Uncultivated Areas and Volunteer Potato	Aerial Spray	Terrestrial	Sheet runoff + spray drift (5%)	0.020	0.80
Control in Wheat, Barley, and Oats		Semi-aquatic	Channelized runoff + spray drift (5%)	0.088	3.5

The risk quotients indicate that if fluroxypyr MHE is transformed to fluroxypyr acid before reaching nontarget plants, then all uses at 0.125 lb ai/A or greater would pose risk to nontarget plants in semiaquatic areas through effects on seedling emergence. Risk to plants in terrestrial habitats would be minimal.

The vigor of nontarget plants can also be harmed through impacts of spray drift on deposition on vegetation. The EEC for spray drift deposition was compared to the vegetative vigor EC<sub>25</sub> to assess this risk. Table 26 gives the RQ for effects on vegetative vigor

Table 26. Exposure and Risk Quotients for Vegetative Vigor Effects on Terrestrial and Semi-aquatic Plants, Based on a Cotton EC<sub>27</sub> of 0.0012 lb ai/A

Use site	Application Method	Rate (lb ai/A)	Spray Drift	EEC (lb ai/A)	Risk Quotients
Wheat, Barley, and Oats	Ground Spray	0.125	1%	0.00125	1 0
	Aerial Spray	0.125	50,0	0.00625	5.2
Uncultivated Areas and Volunteer	Ground Spray	0.25	1%	0.0025	2 1
Potato Control in Wheat, Barley, and Oats	Aerial Spray	0.25	5%	0.0125	10

All risk quotients for vegetative vigor meet or exceed the LOC of 1 for high risk to



nontarget plants. Therefore, spray drift from these uses of fluroxypyr MHE poses a risk to nontarget plants. The risk are marginal for ground applications, but more significant for aerial applications. These uses may harm threatened and endangered species of terrestrial and semiaquatic plants.

#### ii. Aquatic Plants

Fluroxypyr MHE is predicted to degrade rapidly to fluroxypyr acid. However, no acceptable data are available on the toxicity of fluroxypyr acid to aquatic plants. (A supplemental study indicated that fluroxypyr acid has low toxicity to *chlorella vulgaris*, but this is not an acceptable test species for test guideline 123-2.) Therefore, risk to plants was assessed based on the parent compound, fluroxypyr MHE. Because aquatic plant toxicity tests are static, the results reflect some exposure to the fluroxypyr acid as well as fluroxypur MHE.

The risk assessment for aquatic plants is incomplete at this time. The data submitted to the Agency on the toxicity to a freshwater diatom was invalid and thus cannot be used in risk assessment. Risk to aquatic plants could be greater than predicted by this assessment if freshwater diatoms are more sensitive than the other aquatic plants tested.

Risk to aquatic vascular was assessed using the duckweed (*Lemna gibba*) as a model species. Risk to non-vascular aquatic plants was assessed using a blue-green algae, *Anabaena flos-aquae*, which was the most sensitive species nonvascular species tested. Exposure to nontarget aquatic plants may occur through runoff or spray drift from adjacent treated sites. Aquatic EEC's were calculated using the GENEEC program. The risk quotients for nonendangered plants were calculated by dividing the pesticide's peak EEC by the EC<sub>50</sub>. For threatened and endangered vascular plants, risk quotients were calculated by dividing the pesticide's peak EEC by the NOEC for duckweed. There are currently no listed species of nonvascular plants. Table 27 gives the risk quotients for aquatic plants.

Table 27. Risk Quotients for Aquatic Plants Based on Toxicity to a Vascular Plant, Duckweed (Lemna gibba), and a Nonvascular Plant, Marine Diatom (Skeletonema costatum)

		Species	EEC (ppm)	EC.	NOEC	Risk Quotient	
Use Site	Rate (lb ai/A)			EC <sub>so</sub>	NOEC (ppm)	Non-target plants (EEC/EC)	T&E Species (EEC/NOEC)
Wheat, Barley, and Oats	0.125	duckweed	0.0056	> 2.3	1.2	< 0.01	<0.01
<del></del>	·	marine diatom	0.0056	0.29	0.18	0.019	0.031
Uncultivated Areas	0.25	duckweed	0.011	>2.3	1.2	< 0.01	< 10,01 -
Potato Control in Wheat, Barley, and Oats		marine diatom	0.011	0.29	0.18	0.038	0.061

All risk quotients for aquatic plants are below the LOC of 1.0. Thus, these uses of fluroxypyr MHE are predicted to pose minimal risk to aquatic plants, including threatened and endangered species. This assessment is incomplete because data are not available on the toxicity of fluroxypyr MHE on freshwater diatoms.

#### c. Risk Characterization

The parent compound, fluroxypyr MHE, is not predicted to occur in aquatic habitats in significant amounts or for significant duration. Environmental fate information indicates that fluroxypyr MHE rapidly degrades in water to fluroxypyr acid form through hydrolysis and microbial metabolism. Therefore, whenever possible, the risk assessment for aquatic organisms was based on the toxicity of fluroxypyr acid. However, even if this assessment was based on fluroxypyr MHE, the results would still indicate minimal risk to aquatic organisms other than marine/estuarine fish and mollusks. The risk quotients for marine/estuarine fish and mollusks would exceed the LOC for risk to threatened endangered species (0.05) but not the RO for high risk to nonendangered species (0.5). Exposure to fluroxypyr MHE in marine and estuarine environments would be particularly unlikely because saltwater and brackish water tends to be alkaline, and hydrolysis of fluroxypyr MHE to fluroxypyr acid is rapid in alkaline conditions (hydrolysis half-live at pH 9 is 3 days in sterile water). Furthermore, it is likely that much of the fluroxypyr MHE in water would have time to degrade to the acid form before reaching marine or estuarine habitats. In conclusion, EFED has a high confidence in concluding minimal risk to all aquatic organisms, and no significant risk to aquatic threatened and endangered species.

Risk quotients indicate that all uses of fluroxypyr MHE will pose a high risk to terrestrial plants. The predominant risk is from exposure of foliage to spray drift. Risk quotients for ground applications only marginally exceed the LOC, indicating a relatively minor risk. For aerial applications, risk is greater due to the greater amount of spray drift. For this exposure, risk quotients were 5.2 for wheat, oats, and barley and 10 for other uncultivated use sites, as well as volunteer potato control in wheat, barley, and oats. The standard label recommendations for reducing spray drift would help to mitigate this risk.

#### 4. Endangered Species

The proposed uses of furoxypyr MHE on wheat, barley, oats, and uncultivated areas pose a risk to threatened and endangered species of terreatrial plants. They do not pose a significant risk to other threatened and endangered organisms.

#### 5. Labeling Requirements

All producs should contain the following label statements:

"This product is toxic to fish. For terrestrial uses, do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water by cleaning of equipment or disposal of wastes."

#### REFERENCES

- Wan, M.T., D.J. Moul, and R.G. Watts. 1987. Acute toxicity to juvenile pacific salmonids of Garlon 3A<sup>TM</sup>, Garlon 4<sup>TM</sup>, triclopyr, triclopyr ester, and their transformation products: 3,5,6-trichloro-2-pyridinol and 2-methoxy-3,5,6-trichloropyridine. Bull. Environ. Contam. Toxicol. 39:721-728.
- Fletcher, J.S., J.E. Nellessen, and T.G. Pfleeger. 1994. Literature review and evaluation of the EPA food-chain (Kenaga) nomogram, an instrument for estimating pesticide residues on plants. Environ. Toxicol. Chem. Vol.13: pp 1383-1391.
- Hoerger, F. and E.E. Kenaga. 1972. Pesticide residues on plants: correlation of representative data as a basis for estimation of their magnitude in the environment. Environmental Quality and Safety. Vol. 1: pp. 9-28.

## Formulae for Calculating EECs

Terrestrial plants inhabiting areas adjacent to treatment sites

#### Unincorporated ground application:

```
Runoff Loading = maximum application rate (lbs ai/acre) x runoff value Drift Loading = maximum application rate x 0.01

Total Loading = runoff (lb ai/acre) + drift (lb ai/acre)
```

#### Aerial applications:

```
Runoff Loading = maximum application rate (lbs ai/acre) x 0.6 (assumed application efficiency)
x runoff value

Drift = maximum application rate (lbs ai/acre) x 0.05

Total Loading = runoff (lb ai/acre) + drift (lb ai/acre)
```

Semi-aquatic plants inhabiting wet, low-lying areas

#### Unincorporated ground application:

```
Runoff Loading = maximum application rate (lbs ai/acre) x runoff value x 10 acres
Drift Loading = maximum application rate x 0.01
Total Loading = runoff (lb ai/acre) + drift (lb ai/acre)
```

Total Loading = runoff (lb ai/acre) + drift (lb ai/acre)

#### Aerial applications:

```
Runoff = maximum application rate (lbs ai/acre) x 0.6 (60% application efficiency assumed) x runoff value x 10 acres

Drift = maximum application rate (lbs ai/acre) x 0.05
```

Date: 2/24/98 Case No; 060640

Chemical No: 128959/128968-5

#### FLUROXYPYR/FLUROXYPYR MHE DATA REQUIREMENTS FOR ECOLOGICAL EFFECTS

Data Requirements	Composition <sup>1</sup>	Use Pattern <sup>2</sup>	Does EPA Have Data To Satisfy This Requirement? (Yes, No)	Bibliographic Citation	Must Additional Data Be Submitted under FIFRA3(c)(2)(B)?
6 Basic Studies in Bold	•				
71-1(a) Acute Avian Oral, Quail/Duck	TGAI	1,3	Yes	40244514, 40244516, 40244546	No
71-1(b) Acute Avian Oral, Quail/Duck	(TEP)		No ·		No
71-2(a) Acute Avian Diet, Quail	TGAI	1,3	Yes	40244517, 40244547	No
71-2(b) Acute Avian Diet, Duck	TGAI	1,3	Yes	42137301, 42137302	No
71-3 Wild Mammal Toxicity			No		No
71-4(a) Avian Reproduction Quail	TGAI	1,3	Yes	42137303	No
71-4(b) Avian Reproduction Duck	TGAI	1,3	Yes	42137304	No
71-5(a) Simulated Terrestrial Field Study			No .		No
71-5(b) Actual Terrestrial Field Study			No		No
72-1(a) Acute Fish Toxicity Bluegill	TGAI	1,3	Yes	42137306, 44080307	No
72-1(b) Acute Fish Toxicity Bluegilf	(TEP)		No		No
72-1(c) Acute Fish Toxicity Rainbow Trout	TGAI	1,3	Yes	40244518, 40244522, 42137307	No
72-1(d) Acute Fish Toxicity Rainbow Trout	(TEP)		No		No
72-2(a) Acute Aquatic Invertebrate Toxicity	TGAI	1,3	Yes	402444524, 42137308	No
72-2(b) Acute Aquatic Invertebrate Toxicity	(TEP)		No ,		No
72-3(a) Acute Estu/Mari Tox Fish	TGAI	1,3	Yes	44080308, 44080309	No
72-3(b) Acute Estu/Mari Tox Mollusk	TGAI	1,3	Yes	44080310, 44080311	No
72-3(c) Acute Estu/Mari Tox Shrimp	TGAI	1,3	Yes	44080312, 44080313	No

<sup>\*</sup> In Bibliographic Citation column indicates study may be upgradeable

Date: 2/24/98 Case No: 060640 Chemical No: 128959/128968-5 FLUROXYPYR/FLUROXYPYR MHE DATA REQUIREMENTS FOR ECOLOGICAL EFFECTS

Chemical No. 128939/120	300-3			ECOLOGICAL EFFECTS	<del></del>	
Data Requirements		Composition <sup>1</sup>	Use Pattern <sup>2</sup>	Does EPA Have Data To Satisfy This Requirement? (Yes, No)	Bibliographic Citation	Must Additional Data Be Submitted under FIFRA3(c)(2)(B)?
		•	,			
72-3(d) Acute Estu/Mari T	ox Fish	(TEP)		No		No
72-3(e) Acute Estu/Mari Tox Mollusk		(TEP)		No ·		No
72-3(f) Acute Estu/Mari Tox Shrimp		(TEP)		No		No
72-4(a) Early Life-Stage Fish			•	. No		No
72-4(b) Live-Cycle Aquatic Invertebrate				No	•	No
72-5 Life-Cycle Fish				No		No
72-6 Aquatic Org. Accumulation		•		No	44080348	Yes
72-7(a) Simulated Aquatic Field Study				No		No
72-7(b) Actual Aquatic Fie	eld Study			No	•	No
122-1(a) Seed Germ./See	dling Emerg.			No ·		No
122-1(b) Vegetative Vigor	•			No		No
122-2 Aquatic Plant Grow	th			No		No
123-1(a) Seed Germ./See	dling Emerg.	TGAI	1,3	Yes	44080335	No
123-1(b) Vegetative Vigor		TGAI	1,3	Yes	44080335	No ·
123-2 Aquatic Plant Growth		TGAI	1,3	Partial	44080336, 44080337, 44080338, 44080340	Yes¹ .
124-1 Terrestrial Field Stu	dy	•		No		No
124-2 Aquatic Field Study				No .	•	No
141-1 Honey Bee Acute Contact TGAI		1,3	Yes	42137313, 42137314	No	
141-2 Honey Bee Residue on Foliage				No		No
141-5 Field Test for Pollinators				No		No

<sup>&</sup>lt;sup>1</sup>A new quatic plant toxicity test with a freshwater diatom is required to replace an invalid study (MRID 44080339).

\*Composition: TGAI=Technical grade of the active ingredient; PAIRA=Pure active ingredient, radiolabeled; TEP=Typical end-use product

<sup>2</sup>Use Patterns: 1=Terrestrial/Food; 2=Terrestrial/Feed; 3=Terrestrial Non-Food; 4=Aquatic Food; 5=Aquatic Non-Food (Outdoor); 6=Aquatic Non-Food (Industrial); 7=Aquatic Non-Food (Residential); 8=Greenhouse Food; 9=Greenhouse Non-Food; 10=Forestry; 11=Residential Outdoor; 12=Indoor Food; 13=Indoor Non-Food; 14=Indoor Medical; 15=Indoor Residential

# DATA EVALUATION RECORD STUDY 1

CHEM	128959
	14000

Fluroxypyr

§161-2

CAS No. 69377-81-7

FORMULATION--00--ACTIVE INGREDIENT

#### STUDY ID 44080342

Cleveland, C. B. and D. L. Holbrook. The aqueous photolysis of fluroxypyr methylheptyl ester and fluroxypyr (acid) in natural sunlight. Laboratory Study ID: ENV91079. Unpublished study performed and submitted by DowElanco, Midland, MI.

**DIRECT REVIEW TIME = 43.5 Hours** 

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#### **CONCLUSIONS**

### <u>Degradation - Photodegradation in Water</u>

1. This study is scientifically valid and provides useful information on the photodegradation of [2,6-14C]fluroxypyr MHE (4-amino-3,5-dichloro-6-fluoro-pyridyloxyacetic acid, 1-methylheptyl ester) and [2,6-14C]fluroxypyr (4-amino-3,5-dichloro-6-fluoro-pyridyloxyacetic acid), the acid equivalent, in pH 5 aqueous buffer solutions. Although approximately one third of the activity in [2,6-14C]fluroxypyr MHE treated samples was

adsorbed on sample vials during the incubation period, the lack of photolytic degradation does not invalidate the study.

- 2. This study meets Subdivision N Guidelines for the fulfillment of EPA data requirements on photodegradation in water.
- Radiolabeled [2.6-14C] fluroxypyr MHE, at 0.051 ppm, appeared to be stable (registrantcalculated, extrapolated half-life of 197 days) in pH 5 sodium phosphate buffer solution that was irradiated with natural sunlight at approximately 25°C for 34 days. Following 34 days of irradiation, 88.3% of the applied radioactivity remained as parent [2,6-<sup>14</sup>C]fluroxypyr MHE and 1.6% of the applied radioactivity was present as the fluroxypyr acid equivalent. The only confirmed minor degradate at 34 days posttreatment was 4amino-3.5-dichloro-6-fluoro-2-methoxypyridine (methoxypyridine; unspecified concentration). The tentatively identified minor degradate 4-amino-3.5-dichloro-6fluoro-2-pyridinol (dichloropyridinol) was present in one replicate at 34 days posttreatment at approximately 1.1% of the applied radioactivity. An unidentified HPLC peak contained 5% of the applied radioactivity at 34 days posttreatment. In the dark control solutions 98.4% of the applied radioactivity remained as parent [2,6-<sup>14</sup>C]fluroxypyr MHE following 34 days of incubation. In a supplemental study, [2,6-<sup>14</sup>Clfluroxypyr MHE was stable (registrant-calculated, extrapolated half-life of 552 days) in natural water (collected from Brewer Lake, ND) that was irradiated for 28 days under similar conditions.

Radiolabeled [2,6-<sup>14</sup>C]fluroxypyr (acid equivalent), at 0.044 ppm, appeared to be stable (registrant-calculated, extrapolated half-life of 429 days) in pH 5 sodium phosphate buffer solution that was irradiated with natural sunlight at approximately 25 °C for 34 days. Following 34 days of irradiation, 94.7% of the applied radioactivity was present as [2,6-<sup>14</sup>C]fluroxypyr (acid equivalent). The tentatively identified minor degradate 4-amino-3,5-dichloro-6-fluoro-2- pyridinol was present at approximately 2.7% of the applied radioactivity at 34 days posttreatment. An unidentified peak contained 2% of the applied radioactivity at 34 days posttreatment. In the dark control solutions, 98.8% of the applied radioactivity remained as [2,6-<sup>14</sup>C]fluroxypyr (acid equivalent) following 34 days of incubation.

## **METHODOLOGY**

The photolysis of fluroxypyr in aqueous buffer solution was examined at approximately 25 °C using two radiolabeled compounds, [2,6-14C]fluroxypyr MHE (4-amino-3,5-dichloro-6-fluoro-pyridyloxyacetic acid, 1-methylheptyl ester) and [2,6-14C]fluroxypyr, the acid equivalent (4-amino-3,5-dichloro-6-fluoro-pyridyloxyacetic acid), each dissolved in methanol. An additional photolysis study of [2,6-14C]fluroxypyr MHE was performed in a natural water system.

Radiolabeled [2,6-14C] fluroxypyr MHE (radiochemical purity 98.5%, specific activity 25.1 μCi/μmole) was added at a concentration of 0.051 ppm to pH 5 (0.01 M sodium) phosphate) aqueous buffer solution that was sterilized by steam autoclave and to filtersterilized (0.2 µ) natural water (pH 8.2) collected from Brewer Lake, ND. Solutions contained in autoclaved quartz glass vials were shaken for 5 minutes and then incubated at 21.1-26.7°C (monitoring flask or vial temperature) in an outdoor circulating water bath. Control solutions, in vials covered with foil, were shaken and incubated simultaneously with the samples. Temperatures were monitored using temperature probes inserted into the water bath and a sample vial (Figure 2, p. 62). Because volatility of [2,6-14C]fluroxypyr MHE was low, volatile traps were not utilized (pp. 33-34). Samples were irradiated at Midland, MI (43.5° North and 84° West), for 34 days (8/6/91 to 9/9/91) and 28 days (9/12/91 to 10/10/91) for the pH 5 buffer and natural water systems, respectively. The spectral distribution and light intensity were measured using a spectrophotometer: mean irradiance was determined to be 17,973 kJ m<sup>-2</sup> day <sup>1</sup> for the pH 5 buffer system and 11,380 kJ m<sup>-2</sup> day<sup>-1</sup> for the natural water system. Aliquots of both systems were removed for analysis at each sampling interval to determine sterility, pH, and total radioactivity by LSC. Duplicate samples were removed from pH 5 buffer systems for analysis at 0, 7, 17, 24 and 34 days posttreatment and from natural water systems at 0, 4, 8, 15 and 28 days posttreatment.

Radiolabeled [2,6-<sup>14</sup>C]fluroxypyr, the acid equivalent, (radiochemical purity 98.9%, specific activity 27.4 μCi/μmole) was added at a concentration of 0.044 ppm to pH 5 (0.01 M sodium phosphate) aqueous buffer solution that was sterilized by steam autoclave. Samples were shaken and maintained at 15.6-26.6 °C in an incubator under natural sunlight as described above for [2,6-<sup>14</sup>C]fluroxypyr MHE in the pH 5 buffer system; control solution vials were wrapped in foil as described previously. Duplicate samples were removed from pH 5 buffer systems for analysis at 0, 17 and 34 days posttreatment.

Samples were extracted by shaking with methanol. Triplicate aliquots of each test solution were analyzed for total radioactivity by LSC (p.23); detection limits were 1.8 ppb for [2,6-<sup>14</sup>C]fluroxypyr MHE and 1.3 ppb for [2,6-<sup>14</sup>C]fluroxypyr, the acid equivalent (p. 24). Aliquots of each solution were analyzed by reverse-phase HPLC (Waters μ-bondapak C18 column) with a mobile phase gradient (solvent A:solvent B: 80:20 to 40:60 to 0:100, v:v) of H<sub>2</sub>O.glacial acetic acid (990:10, v:v; solvent A) and acetonitrile:glacial acetic acid (990:10, v:v; solvent B); both UV (278 nm) and radioactive flow detection were utilized (pp. 24 and 39). Detection limits for HPLC analyses were 1.8 ppb for [2,6-<sup>14</sup>C]fluroxypyr MHE and 1.3 ppb for [2,6-<sup>14</sup>C]fluroxypyr, the acid equivalent (p. 24). To confirm HPLC results, extracts were separated and analyzed using one-dimensional TLC performed on silica gel plates that were developed in acetonitrile:water:isopropanol (75:20:5, v:v:v; p. 25); detection limits were not reported.

To confirm the sterility of the solutions throughout the incubation period, samples were analyzed for microbial growth at each sampling interval. Culture plates of autoclaved agar were analyzed visually for microbial growth.

#### **DATA SUMMARY**

## [2,6-14C]fluroxypyr MHE

Radiolabeled [2,6-14C]fluroxypyr MHE (radiochemical purity 98.5%), at 0.051 ppm, appeared to be stable (registrant-calculated, extrapolated half-life of 197 days) in pH 5 sodium phosphate buffer solution that was irradiated with natural sunlight at approximately 25 °C (range of 21.1-26.7 °C) for 34 days (Figure 12, p. 72). Degradate concentration data were not presented for the pH 5 buffer systems. Based on results discussed briefly in the text (p. 27), 88.3% of the applied radioactivity was present as parent [2,6-14C]fluroxypyr MHE and 1.6% of the applied radioactivity was present as the fluroxypyr acid equivalent following 34 days of irradiation; however, these data are based on the mean concentration of two replicates, one of which was determined to be nonsterile at 34 days posttreatment (see comment #10). The only confirmed minor degradate in pH 5 buffer solution following 34 days posttreatment was methoxypyridine (unspecified concentration). The tentatively identified minor degradate dichloropyridinol was present in one replicate at 34 days posttreatment at approximately 1.1% of the applied radioactivity. An unidentified HPLC peak contained approximately 5% of the applied radioactivity at 34 days posttreatment; the study authors attributed this peak to multiple components. In the dark control solutions, 98.4% of the applied radioactivity remained as parent [2.6-14Clfluroxypyr MHE following 34 days of incubation. In an additional study, [2,6-14C]fluroxypyr MHE was stable (registrant-calculated, extrapolated half-life of 552 days) in natural water (collected from Brewer Lake, ND) that was irradiated for 28 days under similar conditions. Data for the natural water system are presented in Table VI (p. 43).

Based on LSC data, the material balances throughout the incubation were 89.89% to 103.34% of the applied radioactivity for the pH 5 buffer system (Table VIII, p. 45). Based on HPLC data, the material balances throughout the incubation were 94.8% to 102.6% of the applied radioactivity for the pH 5 buffer system (Table XIII, p. 60).

# [2,6-14C]fluroxypyr (acid equivalent)

Radiolabeled [2,6-14C]fluroxypyr (acid equivalent; radiochemical purity 98.9%), at 0.044 ppm, was stable (registrant-calculated, extrapolated half-life of 429 days) in pH 5 sodium phosphate buffer solution that was irradiated with natural sunlight at approximately 25 °C (range of 15.6-26.6 °C) for 34 days (Figure 13, p. 73). Tabular degradate concentration data were not presented for the pH 5 buffer systems. Based on results discussed briefly in

the text (p. 27), 94.7% of the applied radioactivity was present as [2,6-14C]fluroxypyr (acid equivalent) following 34 days of irradiation. The tentatively identified minor degradate 4-amino-3,5-dichloro-6-fluoro-2- pyridinol was present at approximately 2.7% of the applied radioactivity at 34 days posttreatment. An unidentified peak contained 2% of the applied radioactivity at 34 days posttreatment. In the dark control solutions, 98.8% of the applied radioactivity remained as [2,6-14C]fluroxypyr (acid equivalent) following 34 days of incubation.

Based on LSC data, the material balances throughout the incubation were 100.24% to 102.22% of the applied radioactivity for the pH 5 buffer system (Table VIII, p. 45). Based on HPLC data, the material balances throughout the incubation were 95.2% to 105.3% of the applied radioactivity for the pH 5 buffer system (Table XIII, p. 60).

#### **COMMENTS**

- 1. Complete residue concentration data for the pH 5 buffer systems were not presented in tabular form in the results section. Instead, a brief (partial) discussion of the results were included in the text of the study (p. 27). Parent concentration data are included in Figures 12 and 13 (pp. 32, 33).
- 2. The study authors stated that a minimum of one third of the activity in [2,6
  14C]fluroxypyr MHE treated samples was adsorbed on sample vials during the incubation
  period, and that acceptable radioactivity recoveries were achieved only with the addition
  of methanol after the incubation period and prior to analysis. However, the adsorbance of
  [2,6-14C]fluroxypyr MHE to the glass vials would decrease the effective solution
  concentration during the incubation and affect the study results.
- 3. The reported flask (vial) temperatures for the pH 5 buffer systems treated with the parent compound varied between 21.1 °C and 26.7 °C throughout the incubation (Table XII, pp. 49-54). Although the study authors reported a mean flask temperature of  $24.1 \pm 1.20$  °C, this value was the mean temperature for all data obtained from systems treated either with the parent compound or with the acid equivalent.
- 4. Method validation data were not included in the study.
- 5. Reported registrant-calculated half-lives of [2,6-14C]fluroxypyr MHE and [2,6-14C]fluroxypyr (acid equivalent) in pH 5 buffer solution were 197 and 429 days, respectively. These half-lives were estimated assuming the continuation of the apparent degradation pattern beyond the scope of the observed data. However, data which appear linear may become curvilinear with time.

- The study authors stated that, in a prior investigation, the rapid hydrolysis of [2,6-14C]fluroxypyr MHE to [2,6-14C]fluroxypyr (acid equivalent) was found to be base catalyzed (p. 19), as indicated by half-lives of 3.5, 454 and > 454 days, respectively, for parent fluroxypyr in sterile pH 9, 7 and 5 buffer solutions (incubation conditions not reported).
- 7. A phosphate buffer system (0.01 M sodium phosphate) was utilized to study the photodegradation of [2,6-14C]fluroxypyr MHE and [2,6-14C]fluroxypyr (acid equivalent); it is recommended that borate or acetate buffers be utilized to minimize buffer effects.
- 8. The actual pH of the buffer solutions after sterilization was pH 4.93 (p. 21) and ranged from pH >4.5 to pH <5 during the incubation period (Table III, p. 40).
- 9. Only three sampling intervals were used to determine the half-life of [2,6-<sup>14</sup>C]fluroxypyr (acid equivalent) in pH 5 buffer solutions; a minimum of four sampling intervals is recommended.
- 10. The majority of the samples remained sterile throughout the irradiation period. However, growth occurred on one of the culture plates of the [2,6-14C]fluroxypyr MHE and the [2,6-14C]fluroxypyr (acid equivalent) treated buffer solutions following 34 days posttreatment. The reviewer notes a greater apparent degradation of the parent compound in the non-sterile replicate in comparison with that occurring in the sterile replicate (p. 32). In addition, growth occurred on the edge of the non-irradiated control culture plates of the [2,6-14C]fluroxypyr MHE treated buffer solutions following 24 and 34 days posttreatment.
- 11. Quantum yield was calculated using measured absorbance, molar absorbance, and irradiance values for [2,6-14C]fluroxypyr MHE along with similar measurements from the chemical actinometer p-nitroacetophenone (pp. 29-31). The study authors reported a quantum yield value of 0.0256. This value was calculated using different time and location values (for the actinometer) than those utilized in this study; values were obtained from a data table of solar irradiance in fall at 40 ° North latitude. The study authors stated that this experiment was actually conducted in the late summer (8/6/91 to 9/9/91) at 43.5° North latitude (Midland, MI).
- 12. Pages cited in the review refer to study page numbers on the black line found at the bottom of the page.
- 13. Temperature and solar irradiance data were not collected from 8/28/91 to 8/30/91 due to electrical power failure (pp. 47, 52 and 76).

# DATA EVALUATION RECORD STUDY 2

CHEM 128959	Flurox	§161-3	
CAS No. 69377-81- FORMULATION	- / 00ACTIVE INGREDIENT		
STUDY ID 440803	43		<del></del>
	N. Lubinski. Soil photolysis by Study ID: ENV91080. Unpapolis, IA.		
DIRECT REVIEW	TIME = 44 Hours	· · · · · · · · · · · · · · · · · · ·	
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# CONCLUSIONS

# Degradation - Photodegradation on Soil

1. This study is scientifically valid and provides useful information on the photodegradation of [2,6-14C]fluroxypyr MHE (4-amino-3,5-dichloro-6-fluoro-pyridyloxyacetic acid, 1-methylheptyl ester) on soil.

- 2. This study meets Subdivision N Guidelines for the fulfillment of EPA data requirements on photodegradation on soil.
- Radiolabeled [2,6- $^{14}$ C]fluroxypyr MHE, at a treatment rate of 4 mg/cm², degraded with a registrant-calculated, extrapolated half-life of 152.7 days on air-dried (5.9% moisture content) clay loam soil sample (Barnes loam series) incubated at approximately 25° C for 30 days in natural sunlight. Using the mean fluroxypyr-MHE percent of the applied radioactivity data and first-order linear regression (see comment #15), the extrapolated half-life was estimated to be 119 days ( $r^2 = 0.88$ , n = 6). The discrepancy between half-life estimates should not affect the validity of the study because fluroxypyr-MHE does not significantly photodegrade on soil.

All reported concentration values were means calculated by the reviewer. Parent compound in the irradiated soils decreased from an initial 92.91% of the applied radioactivity to 85.53% by 7 days posttreatment and to 75.01% by 30 days posttreatment. The minor degradate, fluroxypyr (4-amino-3,5-dichloro-6-fluoro-pyridyloxyacetic acid; the acid equivalent), was present at a maximum concentration of 8.89% of the applied radioactivity at 3 days posttreatment. Nonextractable radioactivity in the irradiated soil was a maximum of 2.78% of the applied radioactivity at 14 days posttreatment. Radiolabeled <sup>14</sup>CO<sub>2</sub> accounted for a maximum of 0.16% of the applied radioactivity at 30 days posttreatment. In the dark controls, 79.14% of the applied radioactivity remained as parent [2,6-<sup>14</sup>C]fluroxypyr MHE following 30 days of incubation.

In a supplemental study, radiolabeled [2,6-14C]fluroxypyr MHE, at a treatment rate of 4 mg/cm<sup>2</sup>, degraded with a registrant-calculated half-life of 0.78 days on moist (22.7% moisture content) clay loam soil incubated at approximately 25° C for 32 days in natural sunlight. Sampling intervals were inadequate to accurately establish the half-life of [2,6-<sup>14</sup>C]fluroxypyr MHE on the moist soil. Greater than 50% (87.20% to 6.08%) of the parent compound degraded on the moist soil between 0 and 3 days posttreatment (the next sampling interval). In addition, duplicate samples were not utilized; therefore, halflives and residue concentrations were obtained from single samples. The concentration of parent in the irradiated soils decreased from an initial 87.20% of the applied radioactivity to 6.08% by 3 days posttreatment and to 1.19% by 32 days posttreatment. The major degradate, fluroxypyr (acid equivalent), was present at a maximum concentration of 77.91% of the applied radioactivity at 10 days posttreatment. The minor degradate, 4-amino-3,5-dichloro-6-fluoro-2-pyridinol, was present at a maximum concentration of 0.92% of the applied radioactivity at 10 days posttreatment. Nonextractable radioactivity in the irradiated soil was a maximum concentration of 10.51% of the applied radioactivity at 10 days posttreatment. Radiolabeled volatiles. mainly <sup>14</sup>CO<sub>2</sub>, accounted for a maximum of 0.10% of the applied radioactivity at 10 days posttreatment. In the dark controls, 0.71% of the applied radioactivity remained as parent [2,6-14C]fluroxypyr MHE following 32 days of incubation.

#### **METHODOLOGY**

Subsamples (approximately 2.5 g) of Barnes loam soil (collected from Cass County, ND; 39% sand, 30% silt, 31% clay, 2.52% organic carbon, pH 7.8, CEC 20.1; see comment #6) were weighed into quartz glass round bottom flasks to form a 1-mm layer, treated at 4 mg/cm<sup>2</sup> (mode of application not specified) with [2,6-14C]fluroxypyr MHE (4-amino-3.5-dichloro-6-fluoro-pyridyloxyacetate; radiochemical purity >99%, specific activity 25.1 mCi/mmole), dissolved in acetone, and mixed. Two sample sets were prepared; one sample set was used in an air-dried state (5.9% moisture content) while the second set was moistened to field capacity (22.7% moisture content). The moisture level of the moist soil samples was maintained throughout the incubation. All flasks containing soil samples (except for day 0) were fitted with volatile traps, shaken, and incubated at 19.2-34.2 °C (flask temperature for air-dried samples) or 8.3-33.4 °C (flask temperature for moist samples) in an outside circulating water bath; temperatures were monitored using temperature probes inserted into the water bath and a sample vial (Figure 3, p. 56). Control solutions, in vials covered with aluminum foil, were incubated simultaneously with the samples. Air-dried and moist soil samples were irradiated at DowElanco, Midland, MI (43.37 ° North and 84.13 ° West), for 30 days (6/24/91 to 7/24/91) and 32 days (7/19/91 to 8/20/91), respectively. The spectral distribution and light intensity were measured using a spectrophotometer. Mean daily irradiances were determined to be 23,452 kJ m<sup>2</sup>, 21,415 kJ m<sup>2</sup> and 17,598 kJ m<sup>2</sup> for June, July and August, respectively (Appendix B, p. 69); mean daily irradiances and total irradiance were not reported for each incubation period. Duplicate samples of air-dried and dark control soils were removed for analysis at 0, 1, 3, 7, 14 and 30 days posttreatment. Moist soil samples and dark controls were removed for analysis at 0, 3, 10, 21 and 32 days posttreatment. Duplicate samples of moist soils were not utilized. Soil samples were stored frozen prior to extraction; length and conditions of sample storage were not reported (see Comment #3).

At each sampling interval, soil samples were transferred from the flasks to darkened centrifuge tubes. Soil samples were extracted for one hour by shaking with 1 N HCl:acetone (5:95, v:v) followed by centrifugation; the supernatant was decanted and the extraction procedure was repeated twice (with the addition of vortexing). Post-extracted moist soil samples were air dried and extracted by shaking for 24 hours with 1 N NaOH followed by centrifugation; the supernatant was decanted and the extraction procedure was repeated once. Supernatants were stored frozen (unspecified temperature) until analysis.

Aliquots of the each extract were analyzed by LSC for total radioactivity; detection limits were not reported. Extracts were diluted (1:1, v:v) with distilled, deionized water prior to HPLC analyses. Aliquots of the acetone extracts were analyzed by reverse-phase HPLC (Novapak C18 column) with a mobile phase gradient (solvent A:solvent B: 80:20 to 40:60 to 0:100, v:v) of H<sub>2</sub>O:0.5% acetic acid:0.05% dimethyloctylamine (unspecified

volume ratio; solvent A) and acetonitrile:0.5% acetic acid:0.05% dimethyloctylamine (unspecified volume ratio; solvent B); both UV (254 nm) and radioactive flow detection were utilized (Table V, p. 34). Aliquots of the NaOH extracts (performed only on moist samples) were analyzed by reverse-phase HPLC (Novapak C18 column) with a mobile phase gradient (solvent A:solvent B: 100:0, 60:40, 0:100, v:v) of H<sub>2</sub>O:0.5% acetic acid:0.05% dimethyloctylamine (unspecified volume ratio; solvent A) and acetonitrile:0.5% acetic acid:0.05% dimethyloctylamine (unspecified volume ratio; solvent B); both UV (254 nm) and radioactive flow detection were utilized (Table VI, p. 35). Detection limits were not reported for HPLC analyses.

To determine nonextractable residues, post-extracted soil subsamples were analyzed for total radioactivity using combustion followed by LSC.

Volatile traps containing a polyurethane foam plug, activated carbon and Ascarite (CO<sub>2</sub> absorbent) were analyzed at each sampling interval. The foam plugs and activated carbon were extracted in acetone and analyzed for total radioactivity by LSC. The Ascarite was extracted in distilled, deionized water and analyzed for total radioactivity by LSC (p. 23).

To confirm the viability of the air-dried soil, subsamples of soil were placed in tubes containing sterilized trypticase soy broth and incubated at 25°C for four days. Following incubation, tubes were analyzed visually for microbial growth.

#### DATA SUMMARY

#### Air-dried Soil

Radiolabeled [2,6-14C] fluroxypyr MHE (radiochemical purity >99%), at a treatment rate of 4 mg/cm<sup>2</sup>, degraded with a registrant-calculated, extrapolated half-life of 152.7 days on air-dried clay loam soil (5.9% moisture content) incubated at approximately 25 °C (range of 19.2-34.2 °C) for 30 days in natural sunlight. All reported concentration values were means calculated by the reviewer based on data provided for individual replicates (Table VII, p. 36). The mean concentration of parent in the irradiated soils decreased from an initial 92.91% of the applied radioactivity to 85.53% by 7 days posttreatment, and was present at 75.01% at 30 days posttreatment (Table VII, p. 36). The minor degradate, fluroxypyr (acid equivalent), was present at all sampling intervals with a maximum mean concentration of 8.89% of the applied radioactivity at 30 days posttreatment. Nonextractable radioactivity in the irradiated soil was a maximum of 2.78% of the applied radioactivity at 14 days posttreatment (Table VII, p. 36). Radiolabeled <sup>14</sup>CO<sub>2</sub> accounted for a maximum of 0.16% of the applied radioactivity at 30 days posttreatment (Table VII, p. 36). In the dark controls, 79.14% of the applied radioactivity remained as parent [2,6-14C]fluroxypyr MHE following 30 days of incubation (Tables VIII, p. 37). During the study, the material balances were 96.76-99.87% of the applied radioactivity for the irradiated soil samples (Table VII, p. 36).

#### Moist Soil

Radiolabeled [2,6-14C]fluroxypyr MHE (radiochemical purity >99%), at a treatment rate of 4 mg/cm², degraded with a registrant-calculated half-life of 0.78 days on clay loam soil moistened to field capacity (22.7%) and incubated at approximately 25°C (range of 8.3-33.4 °C) for 32 days in natural sunlight. However, because greater than 50% of the parent compound degraded between 0 and 3 days posttreatment (the next sampling interval), sampling intervals were inadequate to accurately establish the half-life of [2,6-14C]fluroxypyr MHE in this portion of the study. In addition, duplicate samples were not utilized and half-lives and residue concentrations were based on data obtained from single samples. The concentration of parent in the irradiated soils decreased from an initial 87.20% of the applied radioactivity to 6.08% by 3 days posttreatment and to 0% by 21 days. The 21-day posttreatment values were questionable, however, based on the low material balance (82.42%) observed at that interval as well as the slightly greater level of recovered radioactivity (1.19%) observed at 32 days posttreatment (Table IX, p. 38). The major degradate,

4-amino-3,5-dichloro-6-fluoro-pyridyloxyacetic acid (fluroxypyr; the acid equivalent),

was initially present at 15.47% of the applied radioactivity, increased to a maximum concentration of 77.91% at 10 days posttreatment and was present at 74.56% at 32 days posttreatment. The minor degradate, 4-amino-3,5-dichloro-6-fluoro-2-pyridinol, was detected in irradiated soils at 0.65% of the applied radioactivity at 3 days posttreatment and was present at a maximum concentration of 0.92% at 10 days posttreatment; concentrations were determined in the NaOH extract only (Table IX, p. 38). Radioactivity in the NaOH (caustic) extracts was 0.85% of the applied radioactivity at 0 days posttreatment and increased to 33.76% at 32 days posttreatment. Nonextractable radioactivity in the irradiated soil was a maximum concentration of 10.51% of the applied radioactivity at 10 days posttreatment and was 9.22% at 32 days posttreatment (Table IX, p. 38). Radiolabeled volatiles, mainly <sup>14</sup>CO<sub>2</sub>, accounted for a maximum of 0.10% of the applied radioactivity at 10 days posttreatment and were 0.02% at 32 days posttreatment (Table IX, p. 38). In the dark controls, 0.71% of the applied radioactivity remained as parent [2,6-14C]fluroxypyr MHE following 32 days of incubation (Table X, p. 39). During the study, the material balances were 82.42-101.39% of the applied radioactivity for the irradiated soil samples (Tables IX, p. 38).

#### **COMMENTS**

1. Sampling intervals were inadequate to accurately establish the half-life of [2,6-14C]fluroxypyr MHE on the moist soil. Greater than 50% (87.20% to 6.08%) of the

1.5

- parent compound degraded on the moist soil between 0 and 3 days posttreatment (the next sampling interval; Table IX, p. 38).
- 2. The reported flask temperatures for the treated soil samples were not held constant (at the recommended  $25 \pm 1$  °C) throughout the incubation period, but varied from 19.2 to 34.2 °C for the air-dried soil samples and from 8.3 to 33.4 °C for the moist soil samples (Tables XIII and XIV, pp. 44-51). The study authors reported mean flask temperatures of  $25.8 \pm 2.7$  °C for the air-dried soil samples and  $25.1 \pm 2.5$  °C for the moist soil samples (p. 24).
- 3. The study authors stated that flasks of day 0 soil samples were stoppered, covered in aluminum foil and stored in a freezer prior to extraction (pp. 19-20); length and conditions of sample storage were not reported. Storage information concerning samples removed at other intervals was not submitted.
- 4. Detection limits for LSC and HPLC analyses were not reported.
- 5. Replicate soil samples were not utilized to study the photolysis of [2,6-14C]fluroxypyr MHE on moist soil. The use of single samples is generally not considered to be good laboratory practice; at a minimum, duplicate samples should be used.
- 6. Based on sand, silt and clay percentages reported in Table IV, the test sample from the Barnes loam soil is in the clay loam textural class. This variability should not affect the study results.
- 7. The study authors stated that one of the replicates of the air-dried day 30 samples was contaminated with strong caustic from the Ascarite trapping material (p. 26). Therefore, the sample was not used to calculate the half-life of [2,6-14C]fluroxypyr MHE on the air-dried soil.
- 8. The study authors stated that [2,6-14C]fluroxypyr MHE was applied at a rate of 4 mg/cm<sup>2</sup>, an application rate equivalent to one times the field rate of 400 g ai/hectare (p. 18).
- 9. The reported registrant-calculated half-life of [2,6-14C]fluroxypyr MHE on air-dried clay loam soil was 152.7 days. This half-life was estimated assuming the continuation of the apparent degradation pattern beyond the scope of the observed data (Figure 10, p. 63). However, data which appear linear may become curvilinear with time.
- 10. The material balance was questionable for one of the moist soil samples treated with [2,6-14C]fluroxypyr MHE; a recovery of 82.42% of the applied radioactivity was observed at 21 days posttreatment (Table IX, p. 38). The relatively "low" material balance may explain the pattern of decreasing and then increasing concentration of the parent and the major degradate in the soil.

- 11. The reported mean daily irradiance values were 23,452 kJ m² for June, 21,415 kJ m² for July and 17,598 kJ m² for August (appendix B, p. 69). However, mean daily irradiances and total irradiance were not reported for the 30-day (6/24/91 to 7/24/91) air-dried soil study or the 32-day (7/19/91 to 8/20/91) moist soil study. Atmospheric cover and general weather conditions during the incubation periods were not reported.
- 12. In reference to Table IX (p. 38), the reviewer assumed that the degradate pyridinol was 4-amino-3,5-dichloro-6-fluoro-2-pyridinol. In MRID 44094903 (Leaching and Adsorption/Desorption Study), this compound is defined as dichloropyridinol.
- 13. The study authors stated that the soil (Barnes loam) used for this study was the same type as one of the soils used in an unidentified aerobic metabolism study (p. 17).
- 14. An additional photolysis study of [2,6-14C] fluroxypyr MHE on air-dried thick layer soil samples (approximately 10 g) was performed. Four samples (two dark controls) were fitted with volatile traps and incubated in an outside circulating water bath; soils were either shaken several times a day for 15 days or left undisturbed. Results for the shaken and undisturbed samples were determined to be similar by the reviewer (Table XI, p. 40).

# 15. Regression analysis for fluroxypyr-MHE photolysis on soil:

Soil Photo	lysis Study fo	r Fluroxypy	г-МНЕ				
Day	Mean % applied radio.	LN (Mean % ARD)					
	0 92.91	4.5316313				·	
•	1 87.44	4.4709528		Regression		Output:	
	3 84.85	4.440885		Constant			4.4906848
	7 85.53	4.4488672		Std Err of Y Est			0.0270971
1	4 82.55	4.4134042		R Squared			0.8828543
3	75.01	4.3176214		No. of Observations			6
				Degrees of Freedom			4
1-0	91.16	92.91					· .
2-0	94.66			X Coefficient(s)		-0.005832	
1-1	88.07	87.435		Std Err of Coef.		0.0010622	
2-1	86.8						
1-3	83.93	84.85			-0.693	118.832	·
2-3	85.77						
1-7	86.55	85.53			t1/2 = 119		
2-7	84.51						
1-14	80.9	82.555					
2-14	84.21						
1-30	78.36	75.01					
2-30	71.66						

## DATA EVALUATION RECORD STUDY 3

§162-3

CHEM 128959	Fluroxypyi	r		§1
CAS No. 69377-81-	7		·	Ü
FORMULATION	00ACTIVE INGREDIENT			
STUDY ID 440803	14		·	
Cleveland, C. B. and	d J. R. Miller. 1993. Anaerobic a	quati	c metabolism of fluroxypyr	
methylheptyl ester.	Laboratory Study ID: ENV91075	5.1. U	Jnpublished study performed	and
submitted by DowE	lanco, Indianapolis, IN.			
DIRECT REVIEW	TIME = 35 Hours			
REVIEWED BY:	C. A. Little		Signature:	
TITLE: -	Senior Scientist	•	Date:	
EDITED BY:	R. S. Jones		Signature	
TITLE:	Sr. Scientist/Asst. Project Mana	iger	Date:	
APPROVED BY:	P. H. Howard S	ignat	ure:	
TITLE:	Project Manager		Date:	
ORG:	Syracuse Research Corp. Arlington, VA 22202	-	•	•
TEL:	703/413-9369			_
APPROVED BY:	William R. Effland, Ph.D.			•

ORG:

ERB II/EFED/OPP

TEL:

703-305-5738

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## CONCLUSIONS

## Metabolism - Anaerobic Aquatic

- 1. This study is scientifically valid and provides useful information on the anaerobic aquatic metabolism of pyridine ring-labeled [14C-2,6] fluroxypyr MHE (4-amino-3,5-dichloro-6fluoro-2-pyridyloxyacetic acid, 1-methylheptyl ester).
- 2. This study meets Subdivision N Guidelines for the fulfillment of EPA data requirements on anaerobic aquatic metabolism.

Total fluroxypyr [pyridine ring-labeled [14C-2,6] fluroxypyr MHE plus fluroxypyr (acid)], 3. at 0.1 µg/mL (as fluroxypyr MHE), degraded with a registrant-calculated half-life of 8 days (0 to 4 week data) in anaerobic flooded silt loam sediment that was incubated in darkness at 25 °C for up to 12 months. The major degradate fluroxypyr acid was present in the water phase at 11.1% (0.0111  $\mu$ g/mL) of the applied at 1 week posttreatment, and was 0.9-1.7% (0.0009-0.0017  $\mu$ g/mL) of the applied at 2 weeks through 12 months posttreatment. In sediment extracts, the fluroxypyr was 7.6% of the applied radioactivity at day 0, decreased to 2.3% (0.0023  $\mu$ g/mL) of the applied by 1 week posttreatment, and was 0.0-0.5% (0-0.0005  $\mu$ g/mL) at two weeks through 4 months posttreatment. The major degradate 4-amino-3-chloro-6-fluro-2-pyridinol (3-chloropyridinol) was a maximum of 27.2% (0.0272  $\mu$ g/mL) of the applied at 4 months posttreatment, and was 21.5% (0.0215  $\mu$ g/mL) at 12 months posttreatment. In sediment extracts, 3chloropyridinol was a maximum of 4.2% (0.0042  $\mu$ g/mL) of the applied at 4 weeks posttreatment, was not detected at 4 months posttreatment, and was 1.4% (0.0014  $\mu$ g/mL) of the applied at 12 months posttreatment. The major degradate 4-amino-3,5-dichloro-6fluro-2-pyridinol (dichloropyridinol) was a maximum of 54.3% (0.0543  $\mu$ g/mL) of the applied at 2 weeks posttreatment, decreased to 39.1% (0.0391 µg/mL) of the applied by 8 months posttreatment and was 44.5% (0.0445  $\mu$ g/mL) of the applied at 12 months posttreatment. In sediment extracts, dichloropyridinol was a maximum of 11.0% (0.0110  $\mu$ g/mL) of the applied at 4 weeks posttreatment, was 0.9% (0.0009  $\mu$ g/mL) of the applied at 4 months posttreatment, and was not observed at 12 months posttreatment. The minor degradate 4-amino-5-chloro-6-fluro-2-pyridinol (5-chloropyridinol) was a maximum concentration of 5.5% (0.0055  $\mu$ g/mL) by 4 months posttreatment. In sediment extracts, 5-chloropyridinol was 2.9% (0.0029  $\mu$ g/mL) of the applied at 4 weeks posttreatment, decreased to 0.4% (0.0004  $\mu$ g/mL) of the applied by 4 months posttreatment, and was a maximum concentration of 5.9% (0.0059  $\mu$ g/mL) at 12 months posttreatment. Unextracted [14C]residues comprised 27.8% (0.0278 μg/mL) of the applied at 12 months posttreatment. The majority of [ $^{14}$ C]residues (maximum of 82.3% (0.0082  $\mu$ g/mL) at 4 months posttreatment) were observed in the water phase. Radiolabeled <sup>14</sup>CO<sub>2</sub> accounted for 1.2% (0.0012  $\mu$ g/mL) of the applied radioactivity at 12 months posttreatment.

## **METHODOLOGY**

A bulk sample of silt loam sediment (18.7% sand, 64.1% silt, 17.2% clay, 6.4% organic carbon, pH 7.8, CEC 53.2 meq/100 g; Table 6, p. 43) collected from Brewer Lake in Cass County, ND, was placed in a polyurethane bucket, covered with a polyurethane sheet (to minimize air contact) and stored under refrigeration (temperature not specified) until use (p. 20). Five weeks prior to treatment, moist subsamples (10 g dry weight) of sediment were weighed into glass sidearm flasks which each contained 0.2 g of alfalfa. Samples were flooded with 85 mL of natural water (pH 8.2, conductivity 0.51 mmhos/cm, 50 ppm calcium, total dissolved solids 332 ppm; Table 2, p. 39) collected from Brewer Lake near the site of sediment collection; the final sediment water ratio was 1:10. The flasks and

sidearms (Figure 4, p. 58) were sealed and the sediment/water systems were incubated in darkness at 25 °C for five weeks (p. 21). Following the pre-incubation period, the sediment/water samples were measured to determine oxygen content and redox potentials and were then treated with pyridine ring-labeled [14C-2.6] fluroxypyr MHE (4-amino-3.5dichloro-6-fluoro-2-pyridyloxyacetic acid, 1-methylheptyl ester; specific activity 25.1 μCi/μmole, radiochemical purity 99.3%), dissolved in acetone, at a nominal concentration rate of 0.1  $\mu$ g/mL; the pesticide solution was injected into the water layer by syringe (p. 22). Following treatment, 0.2 N NaOH solution was added to the sidearm caustic trap and the flask and sidearm were again sealed. Flasks were incubated anaerobically in darkness at 25 °C for up to 12 months. Samples were removed for analysis at 0 days; 1, 2, 4 and 6 weeks; and 2, 4, 8 and 12 months posttreatment (p. 24; see Comment #3). To determine sediment viability, samples were analyzed once (at an unspecified time) for bacteria using direct microscopy; separate counts of aerobic and anaerobic colonies were not performed. To determine viability of the sediment/water systems throughout the incubation, an aliquot of water removed at each sampling interval was analyzed for microbial activity using Millipore SPC total plate count samplers (p. 30). Additional sediment/water systems were treated at 4 ppm and incubated anaerobically along with the test samples for use in metabolite identification (p. 22). Sterilized (autoclaved five times over a 1.5 month period) sediment samples (2 g) from an aerobic aquatic metabolism study were treated at 0.1 ppm and incubated along with the viable anaerobic test samples to serve as controls (MRID 44080345, p. 21).

All samples and extracts were stored under refrigeration or frozen (temperature not specified) when not in use. All samples were extracted at the time of sampling or within one week of collection; post-extracted soils were combusted within one month of sample collection (Table VII, p. 44).

Sediment and water samples were centrifuged and the water phase was decanted and analyzed in triplicate for total radioactivity by LSC. Aliquots of the water samples were analyzed by reverse-phase HPLC (C18 column) using a mobile phase gradient of (Solvent A) 1% acetic acid in water plus (Solvent B) 1% acetic acid in acetonitrile, both with 0.05% dimethyloctylamine (DMOA; Solvent A:B: 80:20 to 40:60 to 0:100 v:v), to separate fluroxypyr MHE, fluroxypyr and the dichloropyridinol degradate (p. 24; Table IX, p. 46). Eluent fractions were collected and analyzed directly by LSC; cochromatographed reference standards were located using UV (254 nm) detection. Under similar HPLC conditions, a mobile phase gradient of 100:0 to 60:40 to 0:100 (v:v) was used in the identification of the degradates 3- and 5-chloropyridinol (p. 24; Table X, p. 47). The limits of detection for HPLC/LSC analysis of water and soil extracts were 0.03 ppb and 1.6 ppb, respectively; limits of quantitation were four times the limits of detection (p. 25).

Sediment samples were soaked in 1 N HCl for 30 minutes (to dissolve CaCO<sub>3</sub>), and then extracted with acetone: 1 N HCl (95:5, v:v) by shaking for one hour, followed by

centrifugation; the supernatant was decanted and the procedure was repeated three more times (p. 23). Triplicate aliquots of the combined supernatant were analyzed by LSC to determine total radioactivity. Selected samples were diluted with water (1:1, v:v) and analyzed by reverse-phase HPLC as described previously for the water phase samples. Identities of fluroxypyr and other selected degradates were confirmed using GC/MS (RTX5 capillary column) analysis performed in both the EI and negative CI mode (MRID 44080345, p. 33; see Comment #4); the degradates 3- and 5-chlorpyridinol were tentatively identified based on HPLC retention times for reference standards (p. 31). Post-extracted sediment samples were air-dried and analyzed for total radioactivity by LSC following combustion (p. 23).

To determine the presence of anaerobic conditions, the redox potential (E<sub>h</sub>) and dissolved oxygen content were measured prior to treatment and at each sampling interval (p. 22). Redox potentials ranged from -185.5 to -97.7 mV throughout the incubation period and were -117.2 mV at 12 months posttreatment (p. 102). Volatile trap solutions were removed at each sampling interval and analyzed for total radioactivity (as <sup>14</sup>CO<sub>2</sub>) by LSC (p. 23).

#### **DATA SUMMARY**

Total fluroxypyr [pyridine ring-labeled [14C-2,6] fluroxypyr MHE (radiochemical purity 99.3%) plus fluroxypyr (acid)], at a nominal concentration rate of 0.1  $\mu$ g/mL (as fluroxypyr MHE), degraded with a registrant-calculated half-life of 8 days (0 to 4 week data) in anaerobic flooded silt loam sediment that was incubated in darkness at  $25.1 \pm 0.8$ °C for up to 12 months. Unless otherwise noted, all reported concentrations represent data reported for single replicates or are reviewer-calculated means of duplicate samples (as described in Comment #3). Although half-life determinations were calculated using concentration data for fluroxypyr MHE plus fluroxypyr (acid), total concentrations (sums) for the two compounds were not reported, nor were they calculated by the reviewer. Parent [14C-2,6] fluroxypyr MHE in the water phase, based on a tentative identification of the compound determined only from HPLC retention times (see Comment #6), was initially 0.5 % (0.0005  $\mu$ g/mL) of the applied radioactivity at 4 weeks posttreatment, was a maximum concentration of 3.3% (0.0033  $\mu$ g/mL) of the applied at 8 months posttreatment and was 2.3% (0.0023  $\mu$ g/mL) at 12 months posttreatment (Table XIII, p. 50). In sediment extracts, the parent compound was initially present at 78.6%  $(0.0786 \,\mu\text{g/mL})$  of the applied radioactivity at day 0, rapidly decreased to 1.7%  $(0.0017 \,\mu\text{g/mL})$  $\mu$ g/mL) of the applied by 1 week posttreatment, and was not detectable by 12 months posttreatment; sediment extract residue data were not reported for 8 months posttreatment. Parent fluroxypyr MHE was also detected from 4 weeks posttreatment onward at concentrations of up to 0.4% (0.0004  $\mu$ g/mL) of the applied in aliquots of residual water associated with post-centrifuged sediment samples. The major degradate

was initially present in the water phase at 6.0% (0.0060  $\mu$ g/mL) of the applied radioactivity at 0 days posttreatment, increased to 11.1% (0.0111  $\mu$ g/mL) of the applied by 1 week posttreatment, and was present at 0.9-1.7% (0.0009-0.0017  $\mu$ g/mL) of the applied at 2 weeks through 12 months posttreatment. In sediment extracts, the degradate fluroxypyr was initially present at 7.6% (0.0076  $\mu$ g/mL) of the applied radioactivity at day 0, decreased to 2.3% (0.0023  $\mu$ g/mL) of the applied by 1 week posttreatment, and was present at 0.0-0.5% (0-0.0005  $\mu$ g/mL) at 2 weeks through 4 months posttreatment. Fluroxypyr was also detected from 1 week posttreatment onward at concentrations of 0.1-0.2% (0.0001-0.002  $\mu$ g/mL; with one observation of 1.4%) of the applied in aliquots of residual water associated with post-centrifuged sediment samples. In contrast, in sterile control extracts, fluroxypyr MHE was observed at 80.1% (0.0801  $\mu$ g/mL) of the applied radioactivity at 1 month posttreatment while the degradate fluroxypyr accounted for only 3.3% (0.0033  $\mu$ g/mL) of the applied (MRID 44080345; Table XV, p. 54). The major degradate

## 4-amino-3-chloro-6-fluoro-2-pyridinol (3-chloropyridinol)

was initially present in the water phase at 11.3% (0.0113  $\mu$ g/mL) of the applied radioactivity at 1 week posttreatment, was present at concentrations of 16.9-22.7% (0.0169-0.0227  $\mu$ g/mL) of the applied at 2 weeks through 2 months posttreatment, increased to a maximum concentration of 27.2% (0.0272  $\mu$ g/mL) by 4 months posttreatment, and was 21.5% (0.0215  $\mu$ g/mL) of the applied at 12 months posttreatment. In sediment extracts, 3-chloropyridinol was initially present at 2.5% (0.0025  $\mu$ g/mL) of the applied radioactivity at 1 week posttreatment, increased to a maximum concentration of 4.2% (0.0042  $\mu$ g/mL) of the applied by 4 weeks posttreatment, was not detected at 4 months posttreatment, but was then observed at 1.4% (0.0014  $\mu$ g/mL) of the applied at 12 months posttreatment. The degradate 3-chloropyridinol was also detected from 1 week posttreatment onward at concentrations of 1.4-3.3% (0.0014-0.0033  $\mu$ g/mL) of the applied in aliquots of residual water associated with post-centrifuged sediment samples. The major degradate

## 4-amino-3,5-dichloro-6-fluoro-2-pyridinol (dichloropyridinol)

was initially present in the water phase at 51.3% (0.0513  $\mu$ g/mL) of the applied radioactivity at 1 week posttreatment, was present at a maximum concentration of 54.3% (0.0543  $\mu$ g/mL) of the applied at 2 weeks posttreatment, decreased to 39.1% (0.0391  $\mu$ g/mL) of the applied by 8 months posttreatment and was 44.5% (0.0445  $\mu$ g/mL) of the applied at 12 months posttreatment. In sediment extracts, dichloropyridinol was initially present at 8.8% (0.0088  $\mu$ g/mL) of the applied radioactivity at 1 week posttreatment, increased to a maximum concentration of 11.0% (0.0110  $\mu$ g/mL) of the applied by 4 weeks posttreatment, was detected at 0.9% (0.0009  $\mu$ g/mL) of the applied at 4 months

posttreatment, and was not observed at 12 months posttreatment. The degradate dichloropyridinol was also detected from 1 week posttreatment onward at concentrations of 4.3-6.6% of the applied in aliquots of residual water associated with post-centrifuged sediment samples. The minor degradate 4-amino-5-chloro-6-fluoro-2-pyridinol (5-chloropyridinol) was initially present in the water phase at 1.2% (0.0012  $\mu$ g/mL) of the applied radioactivity at 1 week posttreatment, increased to a maximum concentration of 5.5% (0.0055  $\mu$ g/mL) by 4 months posttreatment, and was 3.0% (0.0003  $\mu$ g/mL) of the applied at 12 months posttreatment. In sediment extracts, 5-chloropyridinol was initially present at 1.0% (0.0001  $\mu$ g/mL) of the applied radioactivity at 1 week posttreatment, increased to 2.9% (0.0029  $\mu$ g/mL) of the applied by 4 weeks posttreatment, decreased to 0.4% (0.0004  $\mu$ g/mL) of the applied by 4 months posttreatment, but was then observed at a maximum concentration of 5.9% (0.0059  $\mu$ g/mL) of the applied at 12 months posttreatment. The degradate 5-chloropyridinol was also detected from 1 week posttreatment onward at concentrations of 0.2-0.7% (0.0002-0.0007  $\mu$ g/mL) of the applied in aliquots of residual water associated with post-centrifuged sediment samples.

Unextracted [ $^{14}$ C]residues comprised 27.8% (0.0278  $\mu$ g/mL) of the applied at 12 months posttreatment (Table XI, p. 48). The distribution of [ $^{14}$ C]residues between the sediment and water fractions was not reported, but the majority of residues (maximum of 82.3% (0.0823  $\mu$ g/mL) at 4 months posttreatment) were observed in the water phase (Table XI, p. 48). Total [ $^{14}$ C]radioactivity in the water phase was 69.4-82.3% (0.0694-0.0823  $\mu$ g/ml) of the applied from 1 week through 12 months posttreatment. Total [ $^{14}$ C]radioactivity in the sediment decreased throughout the incubation, from a (after day 0) maximum of 19.3% (0.0193  $\mu$ g/ml) of the applied at 4 weeks posttreatment to 1.5% (0.0015  $\mu$ g/ml) of the applied at 12 months posttreatment. Radiolabeled [ $^{141}$ CO<sub>2</sub> accounted for 1.2% (0.0012  $\mu$ g/ml) of the applied radioactivity at 12 months posttreatment (Table XI, p. 48). Material balances ranged from 92.9% (0.0929  $\mu$ g/ml) to 106.3% (0.1063  $\mu$ g/ml) of the applied radioactivity throughout the study and were 103.2% (0.1032  $\mu$ g/ml) of the applied at 12 months posttreatment (Table XI, p. 48).

## **COMMENTS**

- 1. Method validation data were not submitted. Data from an adequate method validation using fortified samples must be submitted by the registrant.
- 2. The study authors reported that the mean incubation temperature was  $25.1 \pm 0.8$  °C. Because neither raw temperature data nor the range of temperatures observed were reported, the reviewer was unable to confirm whether a relatively constant ( $\pm$  1 °C) temperature was maintained throughout the incubation period.
- 3. The study authors stated that single replicates were collected at four sampling intervals (0 days and 1, 2 and 6 weeks posttreatment) and duplicate samples were collected at all

other sampling intervals. The use of single samples is generally not considered to be good laboratory practice. The study authors also stated that HPLC characterizations were generally performed only once for each phase (water or soil extract) of the sample. It is preferred that multiple (duplicate or triplicate) analyses be performed to ensure the accuracy of the reported data.

- 4. Method details and data pertaining to sterile control samples (which were incubated simultaneously with treated samples) were incorporated by reference. Sterile control sample data were reported in an aerobic aquatic metabolism study (MRID 44080345). Additionally, method details (incomplete) for compound identity confirmation were also incorporated by reference to the MRID listed above. The study authors stated that the anaerobic and aerobic aquatic studies were performed concurrently. The reviewer noted that the laboratory study identification number (ENV91075) at the bottom of the title page of the anaerobic aquatic study (MRID 44080344) was identical to the identification number assigned to the aerobic aquatic study; the correct number appeared to be "ENV91075.1" as displayed at the top right corner of each page within the anaerobic aquatic study.
- 5. Reported data for sampling intervals at which duplicate samples were collected (as noted in Comment #3) represent means calculated by the reviewer. All other reported data represent individual replicates and were obtained directly from the data tables in the study. Concentration data were reported only as "percent of the applied". It is preferred that tabular data also be reported for the actual concentrations (e.g., μg/ml) measured in the test system. Concentration data reported in this DER were calculated by the reviewer by multiplying the nominal application rate by the percent of applied.
- 6. The study authors stated that the (generally increasing) residual fluroxypyr MHE observed with increasing time may have either indicated a biphasic degradation rate or, alternatively, may have resulted from adsorption of the compound to the glass flasks during the incubation (in which case it would have been unavailable for degradation; p. 28). The study authors also noted, however, that the identification of HPLC peak 4 as fluroxypyr MHE was only a tentative identification based on the retention time of the compound (pp. 31, 32). Tentatively identified components were not observed at >10% of the applied radioactivity.
- 7. The study authors stated that there was evidence that the electrode used to determine oxygen content malfunctioned during the course of the study (beginning at approximately two months posttreatment; p. 30). They further stated that all other evidence (redox potential data, sample odor and visual examinations of the sediment color) indicated that anaerobic conditions were maintained throughout the incubation. Neither dissolved oxygen content nor pH data were submitted.
- 8. Table XIII did not include residue concentration data (other than for the degradate

fluroxypyr) for the 0 day water phase sample, but included dash marks in place of numerical values. Because sediment concentration data for day 0 were listed as "0.0%," and because Table VII (p. 44) indicated poor HPLC recoveries from day 0 water samples, the reviewer assumed that the dash marks did not represent non-detectable residues, but rather that data were not available. Clarification by the registrant would be appropriate.

- 9. The study authors stated that a degradate not observed in the (kinetic) test samples was observed in samples treated at an exaggerated rate for the purpose of metabolite identification. The compound was tentatively identified as the dechlorinated pyridinol, 4-amino-6-fluoro-pyridin-2-ol (p. 33).
- 10. The study authors stated that a DT<sub>50</sub> (the time required for the disappearance of 50% of the initial concentration) of 4.5 days was calculated by means of a linear interpolation in the region of interest in the graph depicting the percentage of applied radioactivity at each sampling interval (p. 28).
  - 11. Additional viable sediment/water systems (designated "switch" samples) were treated and incubated anaerobically initially, then later allowed to "become aerobic by mixing with aerobic samples from the sister study" (p. 22). Also, a separate sediment/water system sample set was prepared as described herein, but incubated at 5 °C. Results for the switch samples and for samples incubated at 5 °C were not discussed in this review as they were beyond the scope of the study requirements.
  - 12. The study authors stated that the soil series name for the silt loam sediment was "Rauville loam."
  - 13. Unextracted [<sup>14</sup>C]residues were relatively high, and comprised 12.1% and 27.8% of the applied radioactivity at 4 weeks and 12 months posttreatment, respectively. The study authors stated that bound residue analysis performed for the aerobic aquatic metabolism study (MRID 44080345) indicated that 50-75% of the bound material was classified as humin and that, based on HPLC analysis, the fulvic acid fraction (which contained the majority of the KOH-extractable radioactivity) did not contain fluroyxpyr or pyridinols (for samples incubated under lighted conditions). The study authors further stated that the absence of those compounds in the caustic extracts was evidence that the bound residues were metabolized (radiolabeled) carbon incorporated into microbial cells and organic matter (p. 29).
- The reviewer notes that the registrant-calculated half-life (8 days) was greater than the observed half-life; however, because there were no sampling intervals between day 0 and one week posttreatment, a more accurate estimate of the half-life may not be possible using the reported data.
  - 15. Concentration data were reported only as "percent of the applied". It is preferred that

a last

tabular data also be reported for the actual concentrations (e.g.,  $\mu$ g/ml) measured in the test system.

16. The pH of the test system (8.2) would increase the rate of hydrolytic degradation because fluroxypyr degrades via base-catalyzed hydrolysis.

# DATA EVALUATION RECORD STUDY 4

§162-4

CHEM 128959	Fluroxypy	T .	
CAS No. 69377-81-	-7	•	
FORMULATION	00ACTIVE INGREDIENT		
<del></del>	<del></del>		
STUDY ID 440803			
•	d J. R. Miller. 1993. Aerobic aqu	• • •	
• • •	· ·	5. Unpublished study performed and	1
submitted by Down	lanco, Indianapolis, IN.		
DIRECT REVIEW	TIME = 35 Hours		
REVIEWED BY:	C. A. Little	Signature:	
TITLE:	Senior Scientist	Date:	
EDITED BY:	R. S. Jones	Signature	
TITLE:	Sr. Scientist/Asst. Project Mana	ager Date:	
APPROVED BY:	P. H. Howard S	ignature:	
TITLE:	Project Manager	Date:	
ORG:	Syracuse Research Corp.	·	
	Arlington, VA 22202		
TEL:	703/413-9369		
APPROVED BY:	William R. Effland, Ph.D.	<del></del>	
TITLE:	Environmental Scientist		
ORG:	ERB II/EFED/OPP		

## SIGNATURE:

TEL:

William P. Efflow 3/70/93

703-305-5738

## **CONCLUSIONS**

## Metabolism - Aerobic Aquatic

- 1. This study is scientifically valid and provides useful information on the aerobic aquatic metabolism of pyridine ring-labeled [14C-2;6] fluroxypyr MHE (4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetic acid, 1-methylheptyl ester).
- 2. This study meets Subdivision N Guidelines for the fulfillment of EPA data requirements on aerobic aquatic metabolism.

3. Total fluroxypyr [pyridine ring-labeled [ $^{14}$ C-2,6] fluroxypyr MHE plus fluroxypyr (acid)], at a nominal concentration rate of 0.1  $\mu$ g/ml (as fluroxypyr MHE), degraded with a registrant-calculated half-life of 5.1 days (0 to 4 week data) in aerobic flooded silt loam sediment that was incubated in darkness at 25 °C for up to 12 months. Using the concentration data through the 60-day study period, the aerobic aquatic half-life was estimated to be 14 days [assumed first-order regression of the natural logarithm of the concentration data vs. time (days)]. The 14-day half-life estimate was applied in Tier 1 (GENEEC) modeling. Parent [ $^{14}$ C-2,6] fluroxypyr MHE in the water phase was observed only at day 0, at 0.2% (0.0002  $\mu$ g/ml) of the applied radioactivity. In sediment extracts, the parent compound rapidly decreased from an initial 80.6% (0.0806  $\mu$ g/ml) of the applied radioactivity to 0.7% (0.0007  $\mu$ g/ml) of the applied by 1 week posttreatment and was 0.1% (0.0001  $\mu$ g/ml) at 2 months posttreatment (the final sampling interval for which data were reported).

The major degradate 4-amino-3,5-dichloro-6-fluoro-pyridyloxyacetic acid (fluroxypyr, acid equivalent) was a maximum of 30.9% of the applied at 1 week posttreatment, and was present at 0.8-1.5% (0.0008-0.0015  $\mu$ g/ml) of the applied at 4 weeks through 2 months posttreatment. In sediment extracts, fluroxypyr was present at 14.3% (0.0143)  $\mu$ g/ml) of the applied radioactivity at day 0, decreased to 2.8% (0.0028  $\mu$ g/ml) of the applied by 2 weeks posttreatment, and was present at 0.3-0.9% at 4 weeks through 2 months posttreatment. In contrast, in sterile control extracts, fluroxypyr MHE was 80.1% (0.801 µg/ml) of the applied radioactivity at 1 month posttreatment while the degradate fluroxypyr was 3.3% (0.0033  $\mu$ g/ml) of the applied. The major degradate 4-amino-3chloro-6-fluoro-2-pyridinol (3-chloropyridinol) was present in the water phase at a maximum of 18.0% (0.00180  $\mu$ g/ml) of the applied at 4 months posttreatment, and was 11.8% (0.0118 µg/ml) at 2 months posttreatment. In sediment extracts, 3-chloropyridinol was a maximum of 6.6% (0.0066  $\mu$ g/ml) of the applied at 4 weeks posttreatment, and was 2.2% (0.0022  $\mu$ g/ml) of the applied at 2 months posttreatment. The major degradate 4amino-3,5-dichloro-6-fluoro-2-pyridinol (dichloropyridinol) was initially present in the water phase at a maximum of 44.0% (0.0440  $\mu$ g/ml) of the applied at 2 weeks posttreatment, and decreased to 30.7% and 23.2% (0.0307 and 0.0232  $\mu$ g/ml, respectively) of the applied by 4 weeks and 2 months posttreatment, respectively. In sediment extracts, dichloropyridinol was initially present at 13.2% (0.0132  $\mu$ g/ml) of the applied radioactivity at 1 week posttreatment, decreased to 12.1% (0.0121 µg/ml) of the applied by 4 weeks posttreatment, and was 5.7% (0.0057 µg/ml) of the applied at 2 months posttreatment. Unextracted [ $^{14}$ C]residues comprised 23.7% (0.0237  $\mu$ g/ml) and 38.3% (0.0383  $\mu$ g/ml) of the applied, respectively, at 4 weeks and two months posttreatment. Radiolabeled <sup>14</sup>CO<sub>2</sub> accounted for 3.6% (0.0036 µg/ml) of the applied radioactivity at 4 weeks posttreatment and was 11.4% (0.0114  $\mu$ g/ml) of the applied at 2 months posttreatment.

## **METHODOLOGY**

A bulk sample of silt loam sediment (18.7% sand, 64.1% silt, 17.2% clay, 6.4% organic carbon, pH 7.8, CEC 53.2 meg/100 g; Table 6, p. 44) collected from Brewer Lake in Cass County, ND, was placed in a polyurethane bucket, covered with a polyurethane sheet (to minimize air contact) and stored under refrigeration (temperature not specified) until use (p. 19). Moist subsamples (10 g dry weight) of sediment were weighed into glass sidearm flasks and flooded with 85 mL of natural water (pH 8.2, conductivity 0.51 mmhos/cm, 50 ppm calcium, total dissolved solids 332 ppm; Table 2, p. 40) collected from Brewer Lake near the site of sediment collection; the final sediment:water ratio was 1:10. The flasks were attached to an oxygen manifold and sealed, and the sediment/water systems (Figure 4, p. 70) were pre-incubated aerobically in darkness for two weeks at an unspecified temperature (p. 20). Following the pre-incubation period, the sediment/water samples were treated with pyridine ring-labeled [14C-2,6] fluroxypyr MHE (4-amino-3,5dichloro-6-fluoro-2-pyridyloxyacetic acid, 1-methylheptyl ester; specific activity 25.1 μCi/μmole, radiochemical purity 98.9%), dissolved in acetone, at a nominal concentration rate of 0.1  $\mu$ g/ml; the pesticide solution was injected into the water layer by syringe (p. 18). Following treatment, 0.2 N NaOH solution was added to the sidearm caustic trap and the flask and sidearm were again sealed. Flasks were incubated aerobically in darkness at 25 °C for up to 12 months; aerobic conditions were maintained by means of an oxygen manifold attached to the flasks. Samples were removed for analysis at 0 days; 1, 2, 4 and 6 weeks; and 2, 4, 8 and 12 months posttreatment (p. 23). To determine sediment viability, samples were analyzed once (at an unspecified time) for bacteria using direct microscopy; separate counts of aerobic and anaerobic colonies were not performed. To determine viability of the sediment/water systems throughout the incubation, an aliquot of water removed at each sampling interval was analyzed for microbial activity using Millipore SPC total plate count samplers (pp. 31, 32). Additional sediment/water systems were treated at an exaggerated rate (unspecified) and incubated anaerobically along with the test samples for use in metabolite identification (p. 21). Sterilized (autoclaved five times over a 1.5 month period) sediment samples (2 g) were treated at 0.1 ppm and incubated along with the viable test samples to serve as controls (p. 21). All samples and extracts were stored under refrigeration or frozen (temperature not specified) when not in use (p. 32). All samples were extracted at the time of sampling or within 16 days of collection; post-extracted soils were combusted within 18 days of sample collection (Table VII, p. 45).

Sediment and water samples were centrifuged and the water phase was decanted and analyzed in triplicate for total radioactivity by LSC. Aliquots of the water samples were analyzed by reverse-phase HPLC (C18 column) using a mobile phase gradient of (Solvent A) 1% acetic acid in water plus (Solvent B) 1% acetic acid in acetonitrile, both with 0.05% dimethyloctylamine (DMOA; Solvent A:B: 80:20 to 40:60 to 0:100 v:v), to separate fluroxypyr MHE, fluroxypyr and the dichloropyridinol degradate (p. 23; Table IX, p. 48). Eluent fractions were collected and analyzed directly by LSC; co-

chromatographed reference standards were located using UV (254 nm) detection. Under similar HPLC conditions, a mobile phase gradient of 100:0 to 60:40 to 0:100 (v:v) was used in the identification of the degradate 3-chloropyridinol (p. 23; Table X, p. 49). The limits of detection for HPLC/LSC analysis of water and soil extracts were 0.03 ppb and 1.6 ppb, respectively; the limits of quantitation were four times the limits of detection (pp. 24, 25).

Sediment samples were soaked in 1 N HCl for 30 minutes (to dissolve CaCO<sub>3</sub>), and then extracted with acetone: 1 N HCl (95:5, v:v) by shaking for one hour, followed by centrifugation; the supernatant was decanted and the procedure was repeated three more times (p. 22). Triplicate aliquots of the combined supernatant were analyzed by LSC to determine total radioactivity. Selected samples were diluted with water (1:1, v:v) and analyzed by reverse-phase HPLC as described previously for the water phase samples. To confirm compound identities for fluroxypyr, dichloropyridinol and 3-chloropyridinol, a water sample treated at an exaggerated rate was utilized. For fluroxypyr and dichloropyridinol, an aliquot of the treated water was acidified using 1 N HCl and extracted three times with diethyl ether; extracts were dried with Na<sub>2</sub>SO<sub>4</sub> and evaporated to dryness. For 3-chloropyridinol, an aliquot of the treated water sample was separated using HPLC; eluate fractions were collected, pooled and concentrated using a nitrogen stream. The concentrated sample was "acidified and saturated with NaCl" and extracted with ether (p. 33). Compound identities were confirmed using GC/MS (RTX5 capillary column) analysis performed in both the EI mode and negative CI modes; the degradate 3chlorpyridinol was tentatively identified based on HPLC retention times for reference standards (p. 33). Post-extracted sediment samples were air-dried and analyzed for total radioactivity by LSC following combustion (p. 22).

To determine the presence of aerobic conditions, the dissolved oxygen content was measured at each sampling interval (p. 31). The dissolved oxygen content ranged from 5.7 to 7.6 ppm from 0 days through two months posttreatment (p. 31; no other data reported). Volatile trap solutions were removed at each sampling interval and analyzed for total radioactivity (as <sup>14</sup>CO<sub>2</sub>) by LSC (p. 21). Simultaneous oxidation-reduction potential (Eh) and pH measurements were not reported.

#### **DATA SUMMARY**

Total fluroxypyr [pyridine ring-labeled [ $^{14}$ C-2,6] fluroxypyr MHE (radiochemical purity 98.9%) plus fluroxypyr (acid)], at a nominal concentration rate of 0.1  $\mu$ g/ml (as fluroxypyr MHE), degraded with a regression-estimated half-life of 14 days (0-60 days study-period) or a registrant-calculated half-life of 5.1 days (0 to 4 week data) in aerobic flooded silt loam sediment that was incubated in darkness at 24.6  $\pm$  0.5 °C for up to 12 months (Figure 18, p. 84). Unless otherwise noted, all reported concentrations represent data reported for single replicates or are reviewer-calculated means of duplicate samples

1-1

(as described in Comment #6). Although half-life determinations were calculated using concentration data for fluroxypyr MHE plus fluroxypyr (acid), total concentrations (sums) for the two compounds were not reported. Parent [ $^{14}$ C-2,6] fluroxypyr MHE in the water phase was observed only at day 0, at 0.2% (0.0002  $\mu$ g/ml) of the applied radioactivity (Table XII, p. 51). In sediment extracts, the parent compound was initially present at 80.6% (0.0806  $\mu$ g/ml) of the applied radioactivity at day 0, rapidly decreased to 0.7% (0.0007  $\mu$ g/ml) of the applied by 1 week posttreatment, was 0.8% (0.0008  $\mu$ g/ml) of the applied at 4 weeks posttreatment and was 0.1% (0.0001  $\mu$ g/ml) at 2 months posttreatment, the final sampling interval for which data were reported. The major degradate

4-amino-3,5-dichloro-6-fluoro-pyridyloxyacetic acid (fluroxypyr, acid equivalent)

was initially present in the water phase at 8.4% (0.0084  $\mu$ g/ml) of the applied radioactivity at 0 days posttreatment, increased to a maximum concentration of 30.9% (0.0309  $\mu$ g/ml) of the applied by 1 week posttreatment, and was present at 0.8-1.5% of the applied at 4 weeks through 2 months posttreatment. In sediment extracts, the degradate fluroxypyr was initially present at 14.3% (0.0143  $\mu$ g/ml) of the applied radioactivity at day 0, decreased to 2.8% (0.0028  $\mu$ g/ml) of the applied by 2 weeks posttreatment, and was present at 0.3-0.9% (0.0003-0.0009  $\mu$ g/ml) at 4 weeks through 2 months posttreatment. Fluroxypyr was also detected from 0 days posttreatment onward at concentrations of 0.1-1.2% (0.0001-0.0012  $\mu$ g/ml; with one observation of 3.8%) of the applied in aliquots of residual water associated with post-centrifuged sediment samples. In contrast, in sterile control extracts, fluroxypyr MHE was observed at 80.1% (0.0801  $\mu$ g/ml) of the applied radioactivity at 1 month posttreatment while the degradate fluroxypyr accounted for only 3.3% (0.0033  $\mu$ g/ml) of the applied (Table XV, p. 54). The major degradate

4-amino-3-chloro-6-fluoro-2-pyridinol (3-chloropyridinol)

was initially present in the water phase at 4.0% (0.0040  $\mu$ g/ml) of the applied radioactivity at 1 week posttreatment, increased to a maximum concentration of 18.0% (0.0180  $\mu$ g/ml) by 4 months posttreatment, and was 11.8% (0.0118  $\mu$ g/ml) of the applied at 2 months posttreatment. In sediment extracts, 3-chloropyridinol was initially present at 2.3% (0.0023  $\mu$ g/ml) of the applied radioactivity at 1 week posttreatment, increased to a maximum concentration of 6.6% (0.0066  $\mu$ g/ml) of the applied by 4 weeks posttreatment, and was 2.2% (0.0022  $\mu$ g/ml) of the applied at 2 months posttreatment. The degradate 3-chloropyridinol was also detected from 1 week posttreatment onward at concentrations of 0.5-2.3% (0.0005-0.0023  $\mu$ g/ml) of the applied in aliquots of residual water associated with post-centrifuged sediment samples. The major degradate

4-amino-3,5-dichloro-6-fluoro-2-pyridinol (dichloropyridinol)

was initially present in the water phase at 30.5% (0.0305  $\mu$ g/ml) of the applied radioactivity at 1 week posttreatment, was present at a maximum concentration of 44.0% (0.0440  $\mu$ g/ml) of the applied at 2 weeks posttreatment, and decreased to 30.7% and 23.2% (0.0307 and 0.0232, respectively) of the applied by 4 weeks and 2 months posttreatment, respectively. In sediment extracts, dichloropyridinol was initially present at 13.2% (0.0132  $\mu$ g/ml) of the applied radioactivity at 1 week posttreatment, decreased to 12.1% (0.0121  $\mu$ g/ml) of the applied by 4 weeks posttreatment, and was detected at 5.7% (0.0057  $\mu$ g/ml) of the applied at 2 months posttreatment. The degradate dichloropyridinol was also detected from 1 week posttreatment onward at concentrations of 3.0-5.2% (0.0003-0.0052  $\mu$ g/ml) of the applied in aliquots of residual water associated with post-centrifuged sediment samples.

Unextracted [ $^{14}$ C]residues comprised 23.7% (0.0237  $\mu$ g/ml) of the applied at 4 weeks posttreatment and were 38.3% (0.0383  $\mu$ g/ml) of the applied at 2 months posttreatment (Table XVII, p. 56). The distribution of [ $^{14}$ C]residues between the sediment and water fractions was not reported, but greater residues were observed in the water phase compared with the sediment through 2 months posttreatment (Table XVII, p. 56). Total [ $^{14}$ C]radioactivity in the water phase decreased throughout the incubation from a maximum of 66.2% (0662  $\mu$ g/ml) of the applied at 2 weeks posttreatment to 52.3% and 39.8% (0.0523 and 0.0398  $\mu$ g/ml, respectively) of the applied at 4 weeks and 2 months posttreatment, respectively. Total [ $^{14}$ C]radioactivity in the sediment decreased throughout the incubation, from a (after day 0) maximum of 26.9% (0.0296  $\mu$ g/ml) of the applied at 1 week posttreatment to 21.4% (0.214  $\mu$ g/ml) of the applied at 4 weeks posttreatment and 9.4% (0.0094  $\mu$ g/ml) of the applied at 2 months posttreatment.

Radiolabeled  $^{14}\text{CO}_2$  accounted for 3.6% (0.0036  $\mu$ g/ml) of the applied radioactivity at 4 weeks posttreatment and was 11.4% and 47.7% (0.0114 and 0.0477  $\mu$ g/ml, respectively) of the applied at 2 and 12 months posttreatment, respectively (Table XVII, p. 56). Material balances ranged from 98.2% to 107.1% (0.0982 to 0.1071  $\mu$ g/ml) of the applied radioactivity from 0 days through 2 months posttreatment and were 101.0% (0.1010  $\mu$ g/ml) of the applied at 4 weeks posttreatment (the interval closest to the required 30-day incubation period; Table XVII, p. 56).

#### **COMMENTS**

- 1. Method validation data were not submitted. Data from an adequate method validation using fortified samples must be submitted by the registrant.
- 2. Aerobicity of the samples was not demonstrated beyond the two-month sampling interval due to the malfunctioning of the electrode used to determine oxygen content. However, the required incubation period for an aerobic aquatic metabolism study is 30 days, rather than the 12-month period utilized in this study. The study authors stated that the oxygen

content of the samples ranged from 5.7 to 7.6 ppm during the first two months of the study (p. 31). Neither dissolved oxygen content nor pH data were submitted in tabular form.

- Junextracted [14C]residues were relatively high, and comprised 23.7% and 35.9% of the applied radioactivity at 4 weeks and 12 months posttreatment, respectively, as well as a maximum concentration of 56.4% of the applied at 4 months posttreatment. The study authors stated that bound residue analysis (of samples incubated under lighted conditions) indicated that 50-75% of the bound material was classified as humin and that, based on HPLC analysis, the fulvic acid fraction (which contained the majority of the KOH-extractable radioactivity) did not contain fluroxypyr or pyridinols (p. 28). The study authors further stated that the absence of those compounds in the caustic extracts was evidence that the bound residues were metabolized (radiolabeled) carbon incorporated into microbial cells and organic matter.
- 4. Although samples were collected up to 12 months of incubation, neither water phase samples collected beyond 4 months posttreatment nor soil extracts for samples obtained beyond 2 months posttreatment were analyzed by HPLC (Table VII, p. 45).
- 5. Additional viable sediment/water systems were treated and incubated aerobically in darkness at 5 °C, as well as under lighted conditions at 5 °C and 25 °C (p. 22). Results for these sample sets were not discussed in this review as they were beyond the scope of the study requirements.
- 6. Single samples were analyzed at four sampling intervals (0 days, 1 and 6 weeks, and 8 months posttreatment) and duplicate samples were analyzed at all other sampling intervals. The use of single samples is generally not considered to be good laboratory practice. The study authors also stated that HPLC characterizations were generally performed only once for each phase (water or soil extract) of the sample. It is preferred that multiple (duplicate or triplicate) analyses be performed to ensure the accuracy of the reported data.
- 7. The study authors stated that the low HPLC column recoveries for the 4-month posttreatment water samples were low due to the presence of H<sup>14</sup>CO<sub>3</sub> (in the pH 8.2 water) which was converted to <sup>14</sup>CO<sub>2</sub> (in the acidified HPLC system) and lost due to volatilization (p. 31). The reviewer notes that HPLC recoveries for water samples were reasonable throughout the period of the incubation (4 weeks) during which half-life data was obtained.
- 8. The reviewer notes that the registrant-calculated half-life (5.1 days) was greater than the apparent half-life.
- 9. The study authors reported that the mean incubation temperature was  $24.6 \pm 0.5$  °C (p.

- 31). Because neither raw temperature data nor the range of temperatures observed were reported, the reviewer was unable to confirm whether a relatively constant (± 1 °C) temperature was maintained throughout the incubation period.
- 10. Concentration data were reported only as "percent of the applied". It is preferred that tabular data also be reported for the actual concentrations (e.g.,  $\mu$ g/ml) measured in the test system. Concentration data reported in this DER were calculated by the reviewer by multiplying the nominal application rate by the percent of applied.

## DATA EVALUATION RECORD STUDY 5

§163-1

CHEM 128959	Flurox	ypyr \$16	<b>`</b>
CAS No. 69377-81		310	′-
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STUDY ID 440949	03		
•	<u> </u>	desorption batch equilibrium partitioning o	f
	= 7	es of fluroxypyr. Laboratory Study ID:	
ENV95072. Unpub	olished study performed and su	bmitted by DowElanco, Indianapolis, IA.	
DIRECT REVIEW	TIME = 93 Hours		
REVIEWED BY:	H. L. Evans	Signature:	
TITLE:	Scientist	Date:	
EDITED BY:	C. A. Little	Signature	
TITLE:	Senior Scientist	Date:	
APPROVED BY:	P. H. Howard	Signature:	
TITLE:	Project Manager	Date:	
ORG:	Syracuse Research Corp.		
	Arlington, VA 22202		
TEL:	703/413-9369		
APPROVED BY:	William R. Effland, Ph.D.		
TITLE:	Environmental Scientist		
ORG:	ERB II/EFED/OPP		

SIGNATURE:

TEL:

Willia R. E fflat 3/30/98

## **CONCLUSIONS**

## Mobility - Leaching and Adsorption/Desorption

703-305-5738.

1. This study is not scientifically valid and does not provide useful information on the soil mobility (batch equilibrium) of the fluroxypyr MHE degradate [2,6-14C]dichloropyridinol (4-amino-3,5-dichloro-6-fluoro-2-pyridinol) in four soils or [2,6-14C]methoxypyridine (4amino-3,5-dichloro-6-fluoro-2-methoxypyridine) in four foreign soils. In the dichloropyridinol study, adsorption and desorption residue concentration data were incomplete. More complete results from the adsorption and desorption phases of the

definitive study are needed to examine the soil and solution residue concentrations and the material balances. In addition, one of two replicates of the clay soil treated at 0.020 ppm was lost during the adsorption phase of the study and one of two replicates of the sand soil treated at 0.26 ppm was lost.

In the methoxypyridine study, adsorption and desorption residue concentration data were reported only for the sandy clay loam, silty clay loam and clay loam soil samples treated at 0.1 mg/L and the loamy sand soil samples treated at 0.5 mg/L. In addition, a preliminary study for desorption was not performed and equilibration periods were not determined for three of the four soils utilized.

- 2. This study does not meet Subdivision N Guidelines for the partial fulfillment of EPA data requirements on the soil mobility (batch equilibrium) of the fluroxypyr MHE degradate dichloropyridinol for the following reasons:
  - (i) residue concentration data for adsorption and desorption test solutions were incomplete; and
  - (ii) Freundlich  $K_{\infty}$  values were not reported.
- 3. This study does not meet Subdivision N Guidelines for the partial fulfillment of EPA data requirements on the soil mobility (batch equilibrium) of the fluroxypyr MHE degradate methoxypyridine for the following reasons:
  - (i) complete residue concentration data for adsorption and desorption test solutions were not presented;
  - (ii) the four foreign soils were not characterized using the USDA classification system, and were not adequately compared with domestic (USA) soils;
  - (iii) none of the soils had an organic matter content of less than 1%; and
  - (iv) Freundlich K<sub>des</sub> values were not reported.
- Radiolabeled [2,6-14C]dichloropyridinol, at nominal concentrations of 0.005, 0.020, 0.26 and 5.0 ppm, was determined to be very mobile in sandy loam soil:solution slurries (1:2, w:v) and mobile in silt loam, sand and clay soil:solution slurries (1:2, w:v) that were equilibrated in darkness for approximately 16 hours at 25 °C. Freundlich  $K_{ads}$  values were 4.2 for the sandy loam soil, 28.9 for the silt loam soil, 11.9 for the sand soil and 43.7 for the clay soil; corresponding  $K_{\infty}$  values were not reported. Respective 1/N values were 0.81, 0.87 and 0.85 for adsorption. Freundlich  $K_{des}$  values determined following approximately 22 hours of equilibration were 11.1 for the sandy loam soil, 44.6 for the

silt loam soil, 19.3 for the sand soil and 70.9 for the clay soil; corresponding  $K_{\infty}$  values were not reported. Respective 1/N values were 0.77, 0.79, 0.85 and 0.82 for desorption.

Radiolabeled [2,6-14C]methoxypyridine, at nominal concentrations of 0.05, 0.1, 0.5 and 1.0 mg/L, was determined to be very mobile in foreign loamy sand, clay loam, sandy clay loam and silty clay loam soil:solution slurries (1:5, w:v) that were equilibrated for 1 hour under unspecified incubation conditions. Freundlich  $K_{ads}$  values were 9.28 for the loamy sand soil, 5.93 for the clay loam soil, 7.14 for the sandy clay loam soil and 8.93 for the silty clay loam soil; corresponding  $K_{oc}$  values were 464.0, 312.0, 274.6 and 235.0 mL/g, respectively. Respective 1/N values were 0.96, 0.75, 0.81 and 0.84 for adsorption. Freundlich  $K_{des}$  values were not reported.

#### **METHODOLOGY**

## [2.6-14C]dichloropyridinol

Based on preliminary studies, respective equilibration times of 16 and 22 hours were chosen for the adsorption and desorption of [2,6-14C]dichloropyridinol (4-amino-3,5-dichloro-6-fluoro-2-pyridinol); data were reported in the data analysis and results section of the text (p. 22), but were not presented in tabular form. In a separate preliminary study, adsorption of [2,6-14C]dichloropyridinol to amber test vials was observed to be less than 1%; data were not reported.

For the adsorption phase of the definitive study, aliquots (14 mL) of 0.01 M CaCl<sub>2</sub> solutions containing [2,6-14C]dichloropyridinol (radiochemical purity 96.7%, specific activity 22.5  $\mu$ Ci/ $\mu$ mol), at nominal concentrations of 0.005, 0.020, 0.26 and 5.0 ppm, were added to amber vials containing subsamples (7 g) of sieved (2 mm) Quincy sandy loam, Catlin silt loam, Tavares sand and Pewamo clay soils (Table IV, p. 34); duplicate vials were prepared for each soil type/treatment rate combination. The vials containing the soil:solution slurries were equilibrated on a shaker and maintained in darkness at  $25.16 \pm 0.11^{\circ}$  C for approximately 16 hours (see Comment #7). Following the adsorption equilibration period, soil:solution slurries were centrifuged and the supernatants were decanted. Triplicate aliquots of supernatant from each sample were analyzed for total radioactivity by LSC; the limit of detection and limit of quantitation were 5 dpm and 20 dpm, respectively (p. 21). The pH of the supernatant was measured for one replicate of each sample (Table VI, p. 36). Aliquots of filtered (0.45 mm) supernatant from samples treated at 5.0 ppm were analyzed by reverse-phase HPLC (C18 ODS Hypersil column) using a mobile phase gradient (solvent A:solvent B: 90:10 to 50:50 to 0:100, v:v) of 0.5% glacial acetic acid in water (unspecified volume ratio; solvent A) and 0.5% glacial acetic acid in acetonitrile (unspecified volume ratio; solvent B) with both UV (unspecified wavelength) and radioactive flow detection (pp. 20, 21); the limits of detection and quantitation were 5 dpm and 20 dpm, respectively (p. 21).

For the desorption phase of the definitive study, soil pellets from the adsorption phase of the study were brought to the original weight (soil plus solution) with pesticide-free 0.01 M CaCl<sub>2</sub> (p. 20). Vials containing the soil:solution slurries were placed on a shaker and maintained in darkness at 25.16 ± 0.11 °C for approximately 22 hours (see Comment #7). Following equilibration, soil:solution slurries were centrifuged and aliquots of the supernatants were analyzed for total radioactivity by LSC. Aliquots of filtered (0.45 mm) supernatant from samples treated at 5.0 ppm were analyzed by reverse-phase HPLC as described above. Two additional desorption equilibrations were performed on soil:solution slurries treated at 5.0 mg/L; aliquots of filtered (0.45 mm) supernatant were analyzed by reverse-phase HPLC as described above.

Adsorption and desorption extracts were either analyzed following collection or stored frozen (-20 to -25 °C) for up to one week prior to analysis (p. 20). Following desorption, soil pellets were combusted and analyzed for total radioactivity by LSC.

## [2.6-14C]methoxypyridine

Based on a preliminary study for the adsorption of [2,6-<sup>14</sup>C]methoxypyridine (4-amino-3,5-dichloro-6-fluoro-2-methoxypyridine), an equilibration period of one hour was chosen for the loamy sand soil (Table 12, p. 101); equilibration periods were not determined for the sandy clay loam, silty clay loam and clay loam soils. A preliminary study to determine the equilibration period for the desorption phase was not performed. Based on the results of a preliminary stability study of [2,6-<sup>14</sup>C]methoxypyridine, the study authors stated that the compound was stable in soil:solution slurries; however, no data were not submitted. An additional preliminary study was performed to determine the adsorption of the compound to the glass tubes (see Comment #7; Table 3, p. 91).

For the adsorption phase of the definitive study, aliquots (10 mL) of 0.01 M CaCl<sub>2</sub> solutions containing [2,6-\text{-1}^4C]methoxypyridine (radiochemical purity >99%, specific activity 34.1 mCi/mmol), at nominal concentrations of 0.05, 0.1, 0.5 and 1.0 mg/L (actual concentrations: 0.043, 0.086, 0.42 and 0.76 mg/L, respectively), were added to screw-capped glass tubes containing subsamples (2 g) of sieved (2 mm) foreign Speyer loamy sand, Marcham clay loam, Highworth sandy clay loam and Nimes silty clay loam soils (Non-US soil classifications; see Comment #3); duplicate tubes were prepared for each soil type/treatment rate combination. The tubes containing the soil:solution slurries were equilibrated on a shaker at room temperature for one hour; it could not be determined whether samples were equilibrated in darkness. A blank containing 0.01 M CaCl<sub>2</sub> and four control solutions treated with [2,6-\frac{1}{4}C]methoxypyridine at the same concentrations as the soil:solution slurries were equilibrated along with the samples. Following the adsorption equilibration period, soil:solution slurries were centrifuged and the supernatants were decanted. Aliquots of supernatant from each sample were analyzed for total radioactivity by LSC; detection limits were not reported.

For the desorption phase of the definitive study, soil pellets from the adsorption phase of the study with greater than 25% adsorption were brought to the original weight (soil plus solution) with pesticide-free 0.01 M CaCl<sub>2</sub>. Tubes containing soil:solution slurries were placed on a shaker for 1 hour; the temperature was not specified and it could not be determined whether samples were incubated in darkness. Following equilibration, soil:solution slurries were centrifuged and aliquots of the supernatants were decanted. Aliquots of supernatant from each sample were analyzed for total radioactivity by LSC; detection limits were not reported. An additional desorption equilibration was performed and supernatants were analyzed by LSC.

Following the desorption phase of the definitive study, sandy clay loam, silty clay loam and clay loam soils treated at 0.01 mg/L and loamy sand soil treated at 0.5 mg/L were extracted for one minute by shaking with acetone; extracts were analyzed by LSC and the extraction procedure was repeated twice. After extraction, triplicate subsamples of airdried soil were combusted and analyzed for total radioactivity by LSC (p. 81).

## **DATA SUMMARY**

## [2.6-14C]dichloropyridinol

Radiolabeled [2,6- $^{14}$ C]dichloropyridinol (radiochemical purity 96.7%), at nominal concentrations of 0.005, 0.020, 0.26 and 5.0 ppm, was determined to be very mobile in sandy loam soil:solution slurries (1:2, w:v) and mobile in silt loam, sand and clay soil:solution slurries (1:2, w:v) that were equilibrated in darkness for approximately 16 hours at  $25.16 \pm 0.11$  °C. Freundlich  $K_{ads}$  values were 4.2 for the sandy loam soil, 28.9 for the silt loam soil, 11.9 for the sand soil and 43.7 for the clay soil (Table XIII, p. 43); corresponding  $K_{oc}$  values were not reported. Respective 1/N values were 0.81, 0.81, 0.87 and 0.85 for adsorption. Freundlich  $K_{des}$  values determined following approximately 22 hours of equilibration were 11.1 for the sandy loam soil, 44.6 for the silt loam soil, 19.3 for the sand soil and 70.9 for the clay soil (Tables XIII, p. 43); corresponding  $K_{oc}$  values were not reported. Respective 1/N values were 0.77, 0.79, 0.85 and 0.82 for desorption. Concentration data for [2,6- $^{14}$ C]dichloropyridinol in solution and soil following the adsorption and desorption phases of the definitive study were not reported (other than in units of dpm/mL and dpm/g).

Material balances across all application rates were 85-372% for the clay soil samples, 74-115% for the silt loam soil samples, 88-101% for the sandy loam soil samples and 74-143% for the sand soil samples (Table XIV, p. 44).

## [2.6-14C]methoxypyridine

Radiolabeled [2,6-14C]methoxypyridine (radiochemical purity >99%), at nominal concentrations of 0.05, 0.1, 0.5 and 1.0 mg/L (actual concentrations: 0.0426, 0.0862,

0.4187, 0.7557 mg/L, respectively), was determined to be very mobile in foreign loamy sand, clay loam, sandy clay loam and silty clay loam soil:solution slurries (1:5, w:v) that were equilibrated for 1 hour at room temperature; it could not be determined whether samples were incubated in darkness. Freundlich  $K_{ads}$  values were 9.28 for the loamy sand soil, 5.93 for the clay loam soil, 7.14 for the sandy clay loam soil and 8.93 for the silty clay loam soil (Table 13, p. 102); corresponding  $K_{oc}$  values were 464.0, 312.0, 274.6 and 235.0 mL/g, respectively. Respective 1/N values were 0.96, 0.75, 0.81 and 0.84 for adsorption (Table 13, p. 102). Freundlich  $K_{des}$  values were not reported.

Residue concentration data for [2,6-14C]methoxypyridine in solution and soil samples following the adsorption and desorption phases of the definitive study were reported only for the sandy clay loam, silty clay loam and clay loam soils treated at 0.1 mg/L and the loamy sand soil treated at 0.5 mg/L. During the 1-hour equilibration period, 66.40% of the applied radioactivity was adsorbed to the sandy clay loam soil, 64.41% of the applied was adsorbed to the silty clay loam soil, 69.50% of the applied was adsorbed to the clay loam soil and 62.64% of the applied was adsorbed to the loamy sand soil (Table 14, p. 103). Following desorption, 14.01% of the applied radioactivity was desorbed from the sandy clay loam soil, 13.10% of the applied was desorbed from the silty clay loam soil, 7.30% of the applied was desorbed from the clay loam soil and 24.16% of the applied was desorbed from the loamy sand soil (Table 14, p. 103).

Material balances were 92.64% for the sandy clay loam soil treated at 0.1 mg/L, 86.67% for the silty clay loam soil treated at 0.1 mg/L and 92.70% for the clay loam soil treated at 0.1 mg/L and 94.68% for the loamy sand soil treated at 0.5 mg/L (Table 14, p. 103); material balances were only reported for samples treated at these concentrations.

## **COMMENTS**

## [2.6-14C]dichloropyridinol

- 1. Solution and soil residue concentration data were reported in units of dpm/mL and dpm/g, respectively. The validity of the study could not be adequately assessed because adsorption and desorption residue concentration data were incomplete. Figures 6-7 (pp. 51-52) report incomplete raw and derived concentration data.
- 2. Material balances across all application rates varied with several recoveries falling outside the reasonable range of 90-115% (Table XIV, p. 44). It was unclear whether data from these samples were used for adsorption and desorption coefficient calculations.
- 3. One of two replicates of the clay soil samples treated at 0.020 ppm was lost during the adsorption phase of the study (Table IX, p. 39) and one of two replicates of the sand soil

samples treated at 0.26 ppm was lost (Table XIV, p. 44). The study authors stated that this sample was "lost in processing for mass balance only."

- 4. Freundlich  $K_{oc}$  values were not reported.
- Analysis by HPLC indicated that  $[2,6^{-14}C]$  dichloropyridinol was stable in soil:solution slurries; following the adsorption and desorption phases of the study, mean concentrations of parent compound were  $96.5 \pm 1.4\%$  and  $96.2 \pm 0.9\%$ , respectively (p. 20).
- 7. The study authors stated that adsorption and desorption equilibration periods were  $16 \pm 1$  hours and  $22 \pm 2$  hours, respectively.
- 8. Desorption isotherms of [2,6-14C]dichloropyridinol were plotted using solution concentrations from the first desorption of each application rate utilized as well as by using the solution concentrations of [2,6-14C]dichloropyridinol for each of three successive desorptions for the highest nominal application rate (Figures 10-13, pp. 55-58). Desorption coefficients reported in this review were calculated from desorption isotherms for the first desorption of each application rate. Data obtained from soil samples treated at least four different application rates are required to calculate valid Freundlich desorption coefficients.
- 9. The study authors indicated the Catlin silt loam used for this study was the same type of soil used in an aerobic metabolism study (p. 17).
- 10. The study authors stated that the soils were stored in darkness under refrigeration (temperature unspecified) prior to use (p. 17).
- 11. The study authors stated that the  $K_{\infty}$  values determined for sandy loam, silt loam, sand and clay soils indicated that [2,6- $^{14}$ C]dichloropyridinol has intermediate to low mobility in these soils (p. 26).

## [2.6-14C]methoxypyridine

- Because adsorption and desorption residue concentration data were only reported for the sandy clay loam, silty clay loam and clay loam soil samples treated at 0.1 mg/L and the loamy sand soil samples treated at 0.5 mg/L (Table 14, p. 103), the study is inadequate. More complete results from the adsorption and desorption phases of the definitive study are needed to examine the residue concentrations and material balances.
- 2. A pretiminary study was performed to determine equilibration period for the adsorption of [2,6-14C]methoxypyridine in loamy sand soil (Table 12, p. 101); equilibration periods were not determined for the other three soils. In addition, a preliminary study to

12:

- determine the equilibration period for the desorption of [2,6-14C]methoxypyridine was not performed.
- 3. The Speyer loamy sand soil (Germany), the Marcham clay loam soil (U.K.), the Highworth sandy clay loam soil (U.K.), and the Nimes silty clay loam soil (France) were not characterized using the USDA classification system, nor were they adequately compared with domestic (USA) soils.
- 4. Based on reported carbon content (Table 13 p. 102), at least one of the tested soils did not have an organic matter content of less than 1%.
- 5. Freundlich K<sub>des</sub> values were not reported.
- 6. In the preliminary study performed to determine the adsorption of [2,6-14C]methoxypyridine to the glass tubes, recoveries of 82.7% and 105% of the applied radioactivity were reported (Table 3, p. 91). The study authors stated that adsorption did not occur and that the low recovery (82.7%) of one of the replicates was due to volatile loss (p. 82). However, this was not observed in the second replicate (105%).
- 7. In a preliminary study, analysis by TLC indicated that [2,6-14C]methoxypyridine was stable in CaCl<sub>2</sub> solution during a 16.5-hour equilibration period; concentrations of [2,6-14C]methoxypyridine determined by normal phase and reverse phase TLC were 99.0-99.4% and 100% of the applied, respectively (Table 4, p. 92).
- 8. The study authors stated that the desorption phase of the study was only performed on soil pellets from the adsorption phase of the study with greater than 25% adsorption (p. 77).
- 10. The study authors stated that the soils were stored moist under refrigeration and in darkness prior to use. The study authors also stated that the soils utilized in this study were the same soils used in an aerobic soil metabolism study for fluroxypyr butoxypropyl ester (p. 73).
- The study authors stated that the  $K_{ads}$  and  $K_{oc}$  values determined for the loamy sand, clay loam, sandy clay loam and silty clay loam soils indicated that [2,6-14C]methoxypyridine has intermediate to low mobility in these soils (p. 87).
- 12. The study was conducted under OECD Guideline 106 and was submitted as an appendix (Appendix A) to the [2,6-14C]dichloropyridinol study. The study was very poorly written and organized with regard to details of the methods.

# DATA EVALUATION RECORD STUDY 6

CHEM 128959	Fluroxypyr	§164-1
CAS No. 69377-81-7		
FORMULATION00Emuls	ifiable Concentrate	

#### STUDY ID 44080347

Poletika, N. N., D. W. Roberts, A. M. Phillips, and I. W. Butler. 1996. Terrestrial field dissipation of fluroxypyr. Laboratory Study ID: ENV92023. Unpublished study performed by A & L Great Lakes Laboratories, Inc., Fort Wayne, IN; Agvise, Northwood, ND; DowElanco, Indianapolis, IN; MVTL Laboratories, Inc., New Ulm, MN; Qualls Agricultural Laboratories, Ephrata, WA; and Stewart Agricultural Research Services, Inc., Macon, MO; and submitted by DowElanco.

## STUDY ID 44080355

Phillips, A. M. and B. A. Blakeslee. 1996. Frozen storage stability of fluroxypyr 1-methylheptyl ester, fluroxypyr, 4-amino-3,5-dichloro-6-fluoropyridinol, and 4-amino-3,5-dichloro-6-fluoromethoxypyridine in soil. Laboratory Study ID: RES93010/RES93051. Unpublished study performed and submitted by DowElanco, Indianapolis, IN.

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#### CONCLUSIONS

#### Field Dissipation - Terrestrial

- 1. This study is scientifically valid and provides information on the dissipation of fluroxypyr MHE (4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetic acid, 1-methylheptyl ester) and fluroxypyr (acid equivalent; 4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetic acid) under field conditions in Missouri (MO), North Dakota (ND), and Washington (WA).
- 2. This study does not meet Subdivision N Guidelines for the partial fulfillment of EPA data requirements on the terrestrial field dissipation of fluroxypyr MHE and fluroxypyr (acid) for the following reason:
  - (i) adequate storage stability data were not presented for soils of the test sites, although a storage stability study was conducted (see Comment #1).
- 3. This study may be upgraded with the submission of frozen storage stability data for fluroxypyr MHE, fluroxypyr (acid), and metabolites using soils obtained from the respective test sites.
- 4. Total fluroxypyr residues (fluroxypyr MHE plus fluroxypyr) dissipated in Putnam silty clay loam, Gardena sandy clay loam, and Quincy loamy sand soils in MO, ND, and WA, respectively, with respective registrant-calculated half-lives of 24.8, 36.3, and 13.2 days in plots vegetated with spring wheat (see Comment #7); however, tabular values for total fluroxypyr residues were not submitted. In the 0- to 6-inch soil depth, fluroxypyr MHE was present at maximum concentrations of 29 to 140 ng/g soil by 3 to 7 DAT; fluroxypyr (acid) was observed at maximum concentrations of 180 to 220 ng/g. The metabolite pyridinol (4-amino-3,5-dichloro-6-fluoro-2-pyridinol) was observed at a maximum concentration of 12 ng/g in ND, sporadically at <10 ng/g in WA, and was not detectable in MO. The metabolite methoxypyridine (4-amino-3,5-dichloro-6-fluoro-2-methoxypyridine) was observed at maximum concentrations of 25 to 50 ng/g at all three test sites. Fluroxypyr MHE and its metabolites were not detected below the 6-inch depth, except for methoxypyridine in WA at two months after treatment (2 MAT), which was observed at <10 ng/g in the 6- to 12-inch and 12- to 18-inch soil depths.

In samples obtained from the 0- to 1- or 2-inch depths at each site (0 and 3 DAT only), concentrations of fluroxypyr MHE and fluroxypyr (acid) were substantially higher when compared to the 0- to 6-inch depth.

## **METHODOLOGY**

Fluroxypyr MHE (XRM-5316, 26% a.i.; EC formulation) was broadcast applied as a single postemergence spray at a nominal rate of 0.25 lb acid equivalents (a.e.)/A (1x the proposed maximum rate) onto Putnam silty clay loam, Gardena sandy clay loam, and Quincy loamy sand soils in three field plots (14000-18000 square feet with 6 designated subplots (for sampling) of 15 to 30 feet x 100 feet; pp. 67-69), one each located in MO, ND, and WA; all plots were vegetated with spring wheat. Untreated control plots (2500-6400 square feet) were located at least 147 feet from the treated plots at each site (p. 14). Application rates were not verified directly, but recoveries of total fluroxypyr from soil on the day of application were 76.0%, 88.7%, and 104.8% of the applied (0- to 6-inch depth) in MO, ND, and WA, respectively; respective recoveries were 134.1%, 122.1%, and 127.3% of the applied in the 0- to 2-inch depth (Table VI, p. 34; see Comment #2). Total water input via irrigation and precipitation was 137, 135, and 153% of the 30-year historical precipitation average in MO, ND, and WA, respectively. Pan evaporation data were not reported for any site.

Fifteen soil cores were randomly collected at each sampling interval in two phases. Soil cores (approximately 2.25-inch i.d.) were collected from the 0- to 6-inch depth using a two-stage hydraulic probe with an acetate sleeve (p. 15). A second core (approximately 1.75-inch i.d.) was then collected to a depth of 48 inches. The 6- to 48-inch cores were sectioned into 6-inch increments (p. 16) and all cores were composited by depth increment (into three replicates of five cores each) at each sampling interval. In the control plots, 15 soil cores were collected and combined by depth (6-inch increments) into a single composite sample. At 0 and 3 days after treatment (DAT), 15 additional samples were collected from each site (using a bulb planter) from the 0- to 1- or 2-inch depths and were used in estimating the concentration of fluroxypyr initially present in the soil. All samples were frozen shortly (time interval unspecified) after collection and stored frozen until analysis. To assess the stability of fluroxypyr and its metabolites during shipping and handling, two soil samples from each site were fortified separately with fluroxypyr, pyridinol, and methoxypyridine at 142, 14.2, and 28.4 ng/g fluroxypyr equivalents, respectively (p. 17) at 0 DAT, 1 or 2 DAT, 3 or 4 DAT, 6 months after treatment (MAT), and 12 MAT. The 0 DAT soil samples were also fortified with fluroxypyr MHE at 142 ng/g (fluroxypyr acid equivalents). Mean recoveries for fluroxypyr, pyridinol, and methoxypyridine (averaged across all sampling intervals and study sites) were

 $85\% \pm 33$ ,  $64\% \pm 15$ , and  $96\% \pm 15$ , respectively (p. 19; see Comment #9). The registrant stated that the low recoveries for pyridinol reflected uncertainties in quantifying this analyte at a fortification level (approximately 11.1 ng/g moist soil) that was near its limit of quantitation (10 ng/g oven-dry soil; p. 19). Mean recovery of total fluroxypyr (fluroxypyr MHE plus fluroxypyr acid equivalent) was  $118\% \pm 7$ .

Missouri: Fluroxypyr MHE (XRM-5316, 26.6% a.i.; EC formulation) was applied as a single postemergence spray at 0.25 a.e./A onto a plot (18000 square feet with six designated subplots of 30 feet x 100 feet, 0 to 1% slope; pp. 13, 67) of Putnam silty clay loam soil (7.2% sand, 64.8% silt, 28.0% clay, 1.82% organic matter, pH 7.5, CEC 13.72 meq/100 g; Table 1, p. 28) vegetated with spring wheat at the 1-leaf growth stage near Leonard, MO. A seven-year plot history indicated no prior usage of fluroxypyr or related compounds (p. 14). The depth to the seasonal high water table was estimated by the registrant to be 70 feet (p. 13). Total water input via precipitation and irrigation was 137% of the 30-year historical precipitation average (Table III, p. 31). Environmental conditions were measured at Shelbina, MO, 15 miles from the test site; pan evaporation data were not reported. Soil cores were collected randomly at 0, 3, 7, 14, and 21 DAT, and 1, 2, 3, 4, 5, 6, 10, and 12 MAT (p. 134); samples were stored 81-525 days prior to analysis.

North Dakota: Fluroxypyr MHE (XRM-5316, 26.6% a.i.; EC formulation) was applied as a single postemergence spray at 0.25 a.e./A onto a plot (15600 square feet with six designated subplots of 16.67 feet x 100 feet, 0 to 1% slope; pp. 13, 68) of Gardena sandy clay loam soil (59.2% sand, 16.8% silt, 24.0% clay, 2.87% organic matter, pH 6.2, CEC 15.55 meq/100 g; Table 1, p. 28) vegetated with spring wheat at the 1- to 2-leaf growth stage near Larimore, ND. A seven-year plot history indicated no prior usage of fluroxypyr or related compounds (p. 14). The depth to the seasonal high water table was estimated by the registrant to be 2.5 feet or less (p. 13). Total water input via precipitation and irrigation was 135% of the 30-year historical precipitation average (Table IV, p. 32). Environmental conditions were measured at Grand Forks, ND, 25 miles from the test site; pan evaporation data were not reported. Soil cores were collected randomly at 0, 3, 7, 14, and 21 DAT, and 1, 2, 3, 4, 5, 6, 12, and 18 MAT (p. 134); samples were stored 80-508 days prior to analysis.

Washington: Fluroxypyr MHE (XRM-5316, 26.6% a.i.; EC formulation) was applied as a single postemergence spray at 0.25 a.e./A onto a plot (14400 square feet with six designated subplots of 15 feet x 100 feet, <2% slope; pp. 13, 68) of Quincy loamy sand soil (81.2% sand, 12.8% silt, 6.0% clay, 0.88% organic matter, pH 6.8, CEC 6.80 meq/100 g; Table 1, p. 29) vegetated with spring wheat at the 1- to 2-leaf growth stage near Ephrata, WA. A seven-year plot history indicated no prior usage of fluroxypyr or related compounds (p. 14). The depth to the seasonal high water table was estimated by the registrant to be 47 feet (p. 13). Total water input via precipitation and typical irrigation was 153% of the 30-year historical precipitation average (Table V, p. 33). Environmental conditions were measured at Wenatchee, WA, 25 miles from the test site; pan evaporation data were not reported. Soil cores were collected randomly at 0, 3, 7, 13, and 21 DAT, and 1, 2, 3, 4, 5, 6, and 12 MAT (p. 134); samples were stored 92-693 days prior to analysis.

Soil samples collected from all three field sites were analyzed for fluroxypyr MHE, fluroxypyr (acid), pyridinol, and methoxypyridine. Fluroxypyr MHE was extracted (by shaking) with acetone/0.1 N HCl (90:10, v:v). After evaporation of the acetone, the extract was diluted with additional 0.1 N HCl and applied to a C18 solid phase extraction (SPE) column. The column was dried and residues were eluted with an iso-octane/ether solution (ratios unspecified). The ether was removed by evaporation and the iso-octane extract was analyzed by GC (DB-WAX column; MRID 44080355, p. 12) with electron capture detection (ECD). The method for determining fluroxypyr MHE was designated analytical method ACR 91.10 (p. 121). The limit of detection (LOD) and the limit of quantitation (LOQ) were 8 and 26 ng/g, respectively (p. 123; see Comment #4).

Methoxypyridine, pyridinol, and fluroxypyr (acid) were extracted as described above, except that the method was modified to include a robotic system of extraction (designated analytical method GRM 93.03; pp. 122, 123). For methoxypyridine determinations, the acid extract (remaining after evaporation of the acetone, as described above) was adjusted to a basic pH (unspecified) and extracted with hexane. The hexane extract was applied to a silica gel column and eluted with methyl-t-butyl ether (MTBE); methyoxypyridine residues were extracted into decane and analyzed by GC/MS (DB-5 capillary or DB-1701 columns; MRID 44080355, p. 12) with the detector operating in the selective ion monitoring (SIM) mode. The LOD and LOQ were 4 and 14 ng/g, respectively (p. 123; see Comment #4).

For pyridinol and fluroxypyr determinations (analytical method GRM 93.03; pp. 122, 123), the acid extract (from the initial extraction) was applied to a C18 column and fluroxypyr acid equivalent and pyridinol residues were eluted with ethyl ether:hexane (70:30, v:v). The eluent was diluted with MTBE and separated into two aliquots. From one aliquot, fluroxypyr was extracted with acetone (acidified with phosphoric acid to unspecified pH), derivatized with trimethylsilyl-diazomethane, extracted into toluene, and analyzed by GC/MS (DB-WAX or DB-1701 columns; MRID 44080355, p. 12) with the detector operating in the selective ion monitoring (SIM) mode. The LOD and LOQ were 4 and 12 ng/g, respectively (p. 123; see Comment #4).

The registrant stated that data reported for treated samples were expressed on a fluroxypyr acid equivalent basis and summed across all depths to account for rapid hydrolysis of the parent to fluroxypyr acid and for losses due to leaching (p. 20).

Mean analytical method recovery from 66 soil samples fortified with the parent at 10-500 ng/g was  $104\% \pm 19$  (Table II, pp. 135, 136). Mean recovery of fluroxypyr (acid) from 117 samples fortified at 10-1000 ng/g was  $82 \pm 11\%$  (Table III, pp. 137-140). Mean recovery of pyridinol from 112 samples fortified at 10-200 ng/g was  $101\% \pm 14$  (Table IV, pp. 141-144). Mean recovery of methoxypyridine from 117 samples fortified at 10-200 ng/g was  $95\% \pm 14\%$  (Table V, pp. 145-148). Sample data were corrected for soil

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moisture and method recoveries. Occasional analytical method recovery sample sets were low (see Comment #5).

## Storage Stability Study (MRID 44080355)

In a separate storage stability (MRID 44080355), subsamples (150-200 g) of Catlin silty clay loam soil obtained from Henry County, IL (soil characterization data were not submitted; see Comment #1), were fortified separately with fluroxypyr MHE, fluroxypyr acid equivalent, and pyridinol at 0.10  $\mu$ g/g for each compound (p. 10) and stored frozen (temperature not specified); 20 g soil subsamples were fortified with 0.10  $\mu$ g/g methoxypyridine (see Comment #6). Samples fortified with the parent were analyzed (analytical method ACR 91.10) after 0, 3, 8, 11, 32, 92, 119, 200, and 422 days of storage. Samples fortified with fluroxypyr acid equivalent and pyridinol were analyzed (method GRM 93.03) after 0, 7, 31, 92, 199, 429, and 938 days of storage (pp. 10, 11). Samples fortified with methoxypyridine were analyzed (analytical method GRM 93.03) after 0, 3, 7, 30, 92, 184, 414, and 923 days for storage (pp. 10, 11). Recoveries of parent wee 94-107% after 0-938 days of storage (p. 13); recoveries of pyridinol wee 90-103% after 0-938 days of storage (p. 14); and recoveries of methoxypyridine were 92-108% after 0-923 days of storage. Samples were analyzed in duplicate or triplicate and recovery data were corrected for concurrent procedural recoveries for each compound (pp. 18-29). Samples collected from all three sites were stored frozen (temperature not specified) 80-693 days prior to analysis (pp. 10-14).

#### **DATA SUMMARY**

Fluroxypyr MHE (4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetic, 1 methylheptyl ester) broadcast applied as a single postemergence spray at a nominal rate of 0.25 a.e./A (1x the proposed maximum rate) dissipated (as the sum of the parent plus fluroxypyr acid equivalent) in Putnam silty clay loam, Gardena sandy clay loam, and Quincy loamy sand soils in MO, ND, and WA, respectively, with respective registrant-calculated half-lives of 24.8, 36.3, and 13.2 days in plots vegetated with spring wheat; half-lives were calculated from 0 DAT (see Comment #7). The parent and fluroxypyr (acid) were confined primarily to the 0- to 6-inch soil depth; no data were reported for analyses of the parent below the 6-inch depth at MO and WA. The fluroxypyr metabolites

4-amino-3,5-dichloro-6-fluoro-2-pyridinol (pyridinol) and

4-amino-3,5-dichloro-6-fluoro-2-methoxypyridine (methoxypyridine)

were detected at all three test locations primarily in the 0- to 6-inch soil depth. Total fluroxypyr residues were not reported in tabular form and residue concentration means were not reported for any sampling interval.

Missouri: Total fluroxypyr (fluroxypyr MHE plus fluroxypyr acid) dissipated with a registrant-calculated half-life of 24.8 days in Putnam silty clay loam soil vegetated with spring wheat (Figure 14, p. 48; see Comment #7). In the 0- to 6-inch depth, fluroxypyr MHE was initially observed at soil concentrations of 53 and 75 ng/g (in two of three composite samples), was <26-88 ng/g by 3 DAT, and was <26 and 29 ng/g (in two of three composite samples) at 7 DAT (Table X, pp. 157, 158). Samples were not analyzed for fluroxypyr MHE after 7 DAT.

In the 0- to 6-inch depth, fluroxypyr (acid) was observed at soil concentrations of 94-120 ng/g at 0 DAT, was 100-150 ng/g by 3 DAT, and increased to a maximum of 160-190 ng/g by 7 DAT (Tables XII-XIV, pp. 163, 164). Pyridinol was not detectable in any 6-inch depth increment down to 18 inches. Methoxypyridine was first observed in the 0- to 6-inch depth at <10 ng/g (in two of three composite samples) at 14 DAT, was variable (10-26 ng/g) between 21 DAT and 10 MAT, and was <10 ng/g (in two of three composite samples) at 12 MAT (Tables XIV-XIX, pp. 162-167). Methoxypyridine was not detected below the 6-inch depth.

In samples obtained from the 0- to 1- or 2-inch depths at 0 and 3 DAT, concentrations of the parent and metabolites were substantially higher. In the 0- to 2-inch depth (0 DAT, 15 samples) concentrations of the parent and fluroxypyr acid equivalent were 200-870 ng/g and 350-850 ng/g, respectively (Table X, pp. 157-158; Table XII, p. 160). In the 0-to 1-inch depth (3 DAT, 15 subsamples) concentrations of the parent and fluroxypyr (acid) were 73-390 ng/g and 490-1100 ng/g, respectively; pyridinol was observed at concentrations of <10-17 ng/g (Table X, pp. 157, 158; Table XIII, p. 161). Methoxypyridine was not detectable in the 0- to 1-inch or 2-inch depths at 0 and 3 DAT. The 0- to 1- or 2-inch depths were not analyzed after 3 DAT.

North Dakota: Total fluroxypyr (fluroxypyr MHE plus fluroxypyr acid) dissipated with a registrant-calculated half-life of 36.3 days in Gardena sandy clay loam soil vegetated with spring wheat (Figure 15, p. 49; see Comment #7). In the 0- to 6-inch depth, fluroxypyr MHE was initially observed at soil concentrations of 87-100 ng/g at 0 DAT, was 91-140 ng/g by 3 DAT, and was 51-70 ng/g at 7 DAT (Table XX, pp. 169, 170). Samples were not analyzed for fluroxypyr MHE after 7 DAT.

In the 0- to 6-inch depth, fluroxypyr (acid) was observed at soil concentrations of 70-77 ng/g at 0 DAT, increased to 140-220 ng/g by 7 DAT, and plateaued at 92-160 ng/g between 14 DAT and 1 MAT (Tables XXII-XXV, pp. 172-175). Fluroxypyr acid them decreased to 19-48 ng/g by 2 MAT, <10-14 ng/g by 3 MAT, and was not detectable by 6 MAT (Tables XXVI-XXX, pp. 176-180). Fluroxypyr (acid) was not detected below the 6-inch depth, except at 7 DAT where it was detected at 11-30 ng/g in the 6- to 12-inch depth. Pyridinol was first observed in the 0- to 6-inch depth at <10 ng/g (in one of three samples) at 14 DAT, was <10-12 ng/g at 2 MAT and was not detectable at 3 MAT; pyridinol was not detected below the 6-inch depth at any sampling interval.

Methoxypyridine was first observed in the 0- to 6-inch depth at <10 ng/g at 21 DAT, was variable (24-50 ng/g) between 2 and 14 MAT, and was 21-30 ng/g at 18 MAT. Methoxypyridine was not detected below the 6-inch depth.

In samples obtained from the 0- to 2-inch depth at 0 and 3 DAT, concentrations of the parent and metabolites were substantially higher. In the 0- to 2-inch depth (0 DAT, 15 samples) concentrations of the parent and fluroxypyr (acid) were 210-440 ng/g and 220-420 ng/g, respectively (Table XX, pp. 169, 170; Table XXII, p. 172); pyridinol was observed at concentrations of <10 ng/g (in four of 15 samples). At 3 DAT (15 samples), concentrations of the parent and fluroxypyr acid equivalent were 140-530 ng/g and 240-1600 ng/g, respectively (Table XX, pp. 169, 170; Table XXIII, p. 173). Pyridinol (at 3 DAT) and methoxypyridine (at 0 and 3 DAT) were not detectable. The 0- to 2-inch depths were not analyzed after 3 DAT.

Washington: Total fluroxypyr (fluroxypyr MHE plus fluroxypyr acid) dissipated with a registrant-calculated half-life of 13.2 days in Quincy loamy sand soil vegetated with spring wheat (Figure 16, p. 50; see Comment #7). In the 0- to 6-inch depth, fluroxypyr MHE was initially observed at soil concentrations of 54-72 ng/g at 0 DAT, decreased to <26-47 ng/g by 3 DAT, and was <26 ng/g (composite of 3 samples) at 7 DAT (Table XXXI, pp. 182, 183). Samples were not analyzed for fluroxypyr MHE after 7 DAT. Residue concentration means were not reported.

In the 0- to 6-inch depth, fluroxypyr (acid) was observed at soil concentrations of 120-150 ng/g at 0 DAT, increased to a maximum of 180 ng/g (composite of three samples) by 7 DAT, and decreased to 94-100 ng/g by 14 DAT, 35-44 ng/g by 21 DAT, and <10-16 ng/g (in two of three samples) by 1 MAT, and was not detectable by 2 MAT (Tables XXXIII-XXXVII, pp. 185-189). Fluroxypyr (acid) was not detected below the 6-inch depth, except at 21 DAT where it was detected at <10-14 ng/g in the 6- to 12-inch depth. Pyridinol was first observed in the 0- to 6-inch depth at <10 ng/g between 3 and 21 DAT, and was not detectable at 1 MAT; pyridinol was not detected below the 6-inch depth at any sampling interval. Methoxypyridine was first observed in the 0- to 6-inch depth at <10 ng/g at 14 DAT, was variable (17-25 ng/g) between 21 DAT and 1 MAT, decreased to <10 ng/g by 3 MAT, and was sporadically detected at <10 ng/g between 4 and 12 MAT (Tables XXXVIII-XL, pp. 190-192). Methoxypyridine was not detected below the 6-inch depth, except at 2 MAT where it was observed at <10 ng/g in the 6-12-inch and 12- to 18-inch soil depths.

## **COMMENTS**

1. The soils used in the field dissipation study (MRID 44080347; 0- to 6-inch depth, Table I, pp. 28, 29) were Putnam silty clay loam (MO), Gardena sandy clay loam (ND), and Quincy loamy sand (WA). A Catlin silty clay loam soil from a site in Henry County, IL,

was used to assess the stability of fluroxypyr MHE and its metabolites in frozen storage (MRID 44080355, p.10). The soil used in the storage stability study was not representative of the soils found at the test sites, particularly in ND and WA. Differences in texture, bulk density, moisture content, CEC, pH, and/or microbial populations/activity could differentially affect the stability of the analytes in frozen storage. It is recommended that storage stability studies be conducted using soils obtained from each test site.

2. Application rates were not verified by use of monitoring pads or other valid means. Expected soil concentrations of total fluroxypyr residues were not calculated by the registrant, nor were the soil concentration data expressed as total fluroxypyr residues in tabular form. However, recoveries of total fluroxypyr from soil on the day of application were reported as 76.0%, 88.7%, and 104.8% of the applied (0- to 6-inch depth) in MO, ND, and WA, respectively; respective recoveries were 134.1%, 122.1%, and 127.3% of the applied in the 0- to 2-inch depth (Table VI, p. 34).

In the absence of soil monitoring pad data, application rates may be verified by comparison of the expected 0 DAT soil concentrations of total fluroxypyr residues (fluroxypyr MHE plus fluroxypyr acid) at each site with the measured 0 DAT soil concentrations. The registrant should provide total (summed) residue concentration data for total fluroxypyr in tabular form and calculate mean concentrations for these compounds (and the metabolites) for each sampling interval. The registrant should also calculate the expected concentrations of total fluroxypyr at 0 DAT. Separate calculations of the expected total fluroxypyr concentrations in soil should be made for each site due to differences in soil bulk density.

- Detailed descriptions of the instrumentation used with residue analytical methods ACR 91.10 and GRM 93.03 were not included in the terrestrial dissipation study (MRID 44080347), but were described in the accompanying storage stability study (MRID 44080355).
- 4. The limits of detection (LOD) and limits of quantitation (LOQ) for each analyte were calculated by the registrant from the recovery data obtained from soil samples fortified with each analyte at 10 ng/g (p. 123). The registrant stated that the target LOD and LOQ values (5 and 10 ng/g, respectively) for the fluroxypyr (acid), pyridinol, and methoxypyridine were used in this study because they were the lowest levels at which the samples were fortified with these analytes (pp. 123, 124). For fluroxypyr MHE (the parent), the registrant-calculated statistical values for LOD and LOQ (8 and 26 ng/g, respectively) were used in this study because they were higher than the target values.
- 5. Concurrent analytical method recoveries of the parent and its metabolites from soil samples fortified separately with each analyte at 10-500 ng/g soil were variable. Field sample data were corrected for method recoveries on their respective days of analysis.

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Analytical method recoveries of fluroxypyr MHE from 66 soil samples fortified at 10-300 ng/g were 46-142% of the applied (Table II, pp. 135, 136), including one set of six samples that were 46-96% (p. 136); recoveries from 53 of 66 samples were ≥70% and ≤120%.

Analytical method recoveries of fluroxypyr (acid) from 117 samples fortified at 10-500 ng/g were 58.6-118.2% of the applied (Table III, pp. 137-140); recoveries from 100 of 117 samples were  $\geq$ 70% and  $\leq$ 120%.

Analytical method recoveries of pyridinol from 112 samples fortified at 10-200 ng/g were 60.9-128.6% of the applied (Table IV, pp. 141-144); recoveries from 102 of 112 samples were  $\geq 70\%$  and  $\leq 120\%$ .

Analytical method recoveries of methoxypyridine from 117 samples fortified at 10-200 ng/g were 53.8-128.0% of the applied (Table V, pp. 145-148); recoveries from 112 of 117 samples were  $\geq$  70% and  $\leq$  120%.

- 6. Soil subsamples to be fortified with fluroxypyr MHE, fluroxypyr (acid), and pyridinol (150-200 g) were initially weighed into plastic bags, separately fortified with each compound (dissolved in acetone) at  $0.10 \mu g/g$  soil, and transferred to metal paint cans prior to frozen storage. The registrant stated that due to the volatility of methoxypyridine, 20-g subsamples of soil were weighed directly into the metal paint cans, then fortified with  $0.10 \mu g$  methoxypyridine/g soil.
- 7. The registrant assumed first-order dissipation kinetics for total fluroxypyr residues (fluroxypyr MHE plus fluroxypyr) at each site and plotted best-fit curves. Half-lives were calculated from 0 DAT as well as from the sampling interval where peak concentrations (3 or 7 DAT) of total fluroxypyr were observed. Half-lives calculated from the 0 DAT sampling interval were reported above. Half-lives calculated using the peak concentration sampling intervals as time = 0 were 9.0 or 16 days, 14.3 or 21.3 days, and 9.6 or 12.6 days in MO, ND, and WA, respectively. The two values reported for each site reflect discrepancies between the half-lives reported in Figures 14-16 (first value; pp. 48-50) and the text (second value; p. 22). No explanation was provided for the discrepancies in the reported half-lives between the Figures 14-16 and the text (p. 22). Additionally, dissipation curves were presented as the disappearance of the "percent of applied, on an acid equivalent (a.e.) basis." It is not clear whether the half lives of total fluroxypyr were calculated using the "percent of applied" values or using the measured total fluroxypyr soil concentrations. Clarification of this issue by the registrant is necessary.

Additionally, because half-life calculations were determined based on the dissipation of fluroxypyr MHE plus fluroxypyr (acid), the registrant should provide total (summed)

- residue concentration data for total fluroxypyr in tabular form and report mean concentrations for these compounds (and the metabolites) for each sampling interval.
- 8. It is preferred that soil residue concentration data be presented in tabular form as the mean concentrations of all the replicates for a given sampling interval, in addition to the values presented for the individual replicates.
- 9. Field spike recoveries for all analytes across all sites and sampling intervals were extremely variable. Recoveries of fluroxypyr (acid), pyridinol, and methoxypyridine ranged 35% to 241%, 34% to 85%, and 65% to 116%, respectively (Tables XLI-LVI, pp. 194-209). The impact on the study of unusually low or high recoveries of analytes from field spike samples at particular sampling intervals was not discussed by the registrant.

# DATA EVALUATION RECORD STUDY 7

CHEM 128959	Fluroxypyr	§165-4
CAS No. 69377-81-7	Тигокуруг	2102 1
FORMULATION00ACTI	VE INGREDIENT	
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### STUDY ID 44080348

Rick, D. L., H. D. Kirk, D. D. Fontaine and K. B. Woodburn. 1996. The bioconcentration and metabolism of fluroxypyr 1-methylheptyl ester by the rainbow trout, *Oncorhynchus mykiss* Walbaum. Laboratory Study ID: DECO-ES-2679. Unpublished study performed by The Dow Chemical Company, Midland, MI; and submitted by DowElanco, Indianapolis, IN.

DIRECT REVIEW TIME = 63 Hours C. A. Little REVIEWED BY: Signature: Senior Scientist TITLE: Date: R. S. Jones EDITED BY: Signature TITLE: Sr. Scientist/Asst. Project Manager APPROVED BY: P. H. Howard Signature: TITLE: Project Manager Date: ORG: Syracuse Research Corp. Arlington, VA 22202

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### **CONCLUSIONS**

#### Laboratory Accumulation - Fish

1. This study is of questionable validity and does not provide useful information on the bioaccumulation of fluroxypyr MHE (4-amino-3,5-dichloro-6-fluoro-2-pyridinyloxyacetic acid, 1-methylheptyl ester) in fish. While a method validation study indicated that HPLC column recoveries of radioactivity from fish tissue extracts were adequate, column recoveries of radioactivity from fortified water samples were only 67%

and 65% of the applied for samples analyzed at 30 minutes and 24 hours posttreatment, respectively. Because reported aqueous concentration data represented adjusted values (to account for parent compound loss presumed to have occurred during column injection), bioconcentration factors (BCF) based on the aqueous concentration of the parent compound are questionable. Additionally, the aqueous concentration of the parent compound was not constant, but varied from 0.168 to 0.42 ng/mL throughout the exposure period.

- 2. This study does not meet Subdivision N Guidelines for the fulfillment of EPA data requirements on bioaccumulation in fish for the following reasons:
  - (i) rainbow trout were used to study the bioaccumulation of fluroxypyr MHE in a laboratory setting; the recommended species is either bluegill sunfish or channel catfish;
  - (ii) the analytical method was inappropriate and could not adequately recover the parent compound or its degradates from water samples;
  - (iii) the aqueous concentration of the pesticide (in the form of the parent compound) was not reasonably constant, but varied between 11% and 29% of the nominal application (based on values adjusted to correct for method inadequacies); and
  - (iv) complete tissue concentration data (for the parent compound and the major degradate) were not reported for each tissue type and sampling interval.
- 3. Radiolabeled residues accumulated in rainbow trout that were exposed to pyridine ringlabeled [14C-2,6] fluroxypyr MHE at approximately 1.5 ng/mL (with a mean parent compound concentration of only 0.3 ng/mL and the remainder attributed to the degradate fluroxypyr acid), with maximum total radioactivity bioconcentration factors of 6.06x for edible (muscle), 53.87x for nonedible (head, skin, viscera and skeleton) and 62.11x for whole fish tissues (based on reviewer calculations). However, the aqueous concentration of parent compound was variable and the analytical method for the determination of the parent compound in aqueous solution was questionable; concentrations of [14C]residues in fish tissues were also variable with time. The only major degradate observed in each tissue type was the hydrolysis product fluroxypyr (acid); complete residue concentration data were not reported. Depuration was rapid, with the accumulated [1'C]residues eliminated from the edible fish tissues by day 3 and from the whole fish tissues by day 7; depuration of accumulated residues from nonedible tissues was variable. However, no [14C]residues were detected in day 1 through day 4 depuration period water samples; no other water samples were collected during depuration.

### **METHODOLOGY**

Prior to study initiation, rainbow trout (*Oncorhynchus mykiss* Walbaum) eggs were fertilized in the laboratory under red light, transferred to a salmonid hatcher and incubated at approximately 11.5 °C; embryos were held in the hatcher until the majority initiated swim-up activity (pp. 12, 13). The fish were then transferred to holding tanks containing sand-filtered, dechlorinated (with activated charcoal), irradiated (UV) Lake Huron feed water (12° C, hardness 67-80 mg/L as CaCO<sub>3</sub>, alkalinity 46-57 mg/L as CaCO<sub>3</sub>, pH 7.7-7.9, conductivity 230-260 µmhos/cm) and were fed a standard laboratory diet until they reached a body weight of 0.3-0.5 g. All fish were acclimated for at least 14 days prior to study initiation.

Flow-through aquatic exposure systems were prepared using two 43-L glass aquaria lined with Teflon bags (0.005-inch thickness) to minimize adsorption of the test compound to the glass. The test water (described above) was continuously supplied at a mean measured flow rate of 255 L/day (177 mL/min; approximately 6 turnovers/day). Five days prior to the introduction of fish into the aquaria, the exposure tank was treated with pyridine ring-labeled [ $^{14}$ C-2,6] fluroxypyr MHE (4-amino-3,5-dichloro-6-fluoro-2-pyridinyloxyacetic acid, 1-methylheptyl ester; specific activity 26.7 mCi/mmole, radiochemical purity 98.5%), dissolved in dimethylformamide (DMF), at a nominal concentration of 1.5 ng/mL; the compound was introduced into the test water by injection with a syringe pump adjusted to deliver a constant nominal flow rate ( $10 \mu$ L/min). The control tank was treated only with DMF at a concentration (<0.1 mL/L) similar to that occurring in the exposure tank. The aquaria were placed in a water trough and maintained at  $12 \pm 2$  °C; fluorescent lighting was used with a photo/dark period of 16 hours/8 hours per day.

Rainbow trout (306; mean weight  $0.38 \pm 0.11$  g, length not specified) were placed into each aquarium and the aquaria were covered with plexiglass lids and continuously aerated to maintain a dissolved oxygen content of >60% of saturation (p. 14). The fish were fed a standard laboratory diet; uneaten food and fecal matter were generally removed by siphoning approximately one hour after feeding or as required. During the exposure period, four fish were collected at days 0, 1, 3, 7, 10, 14, 16, 21 and 28 to determine total radioactivity in whole fish tissues; four additional fish were collected at each interval for the determination of total radioactivity in the edible (muscle) and nonedible (head, skin, viscera and skeleton) tissue. Additional fish (number unspecified) were collected at exposure days 3, 7, 14, 16, 21 and 28 for the characterization of radiolabeled residues in whole fish, edible and nonedible tissues. Water from each aquarium was sampled daily during the uptake phase of the study to determine temperature, flow rates and total radioactivity. Water samples obtained at sampling intervals described for fish were also analyzed for dissolved oxygen and pH. Duplicate samples were obtained from the control tank, with the exception of triplicate samples removed on exposure days 19-21, while six replicate samples were obtained from the exposure tank at most sampling

intervals (not including weekend or depuration days on which triplicate samples were removed). Single samples were obtained from the mixing (dosing) chamber daily, with the exception of exposure days 5 and 6.

Following a 28-day exposure period, fish from the treated and control aquaria were respectively transferred to clean aquaria for a 17-day depuration period. Fish were collected at depuration days 0.5, 1, 3, 7, 10, 14 and 17 for the determination of total radioactivity in the edible (muscle) and nonedible (head, skin, viscera and skeleton) tissue. During the depuration period, water samples were collected daily from each aquarium for the first four days only to determine total radioactivity; water sampling was terminated after four days of depuration due to the lack of radioactivity observed in the water.

Because incomplete dissolution of the lipophilic test substance was anticipated, despite the use of DMF and a concentration of parent material below the water solubility of the compound, water samples (from each tank and the mixing chamber) were centrifuged prior to analysis to ensure only the detection of dissolved test material. Water samples and mixing chamber samples collected daily were analyzed directly for total radioactivity by LSC (p. 15); the method detection limit was 0.01 ng/mL. To characterize radioactivity in water samples, selected samples were centrifuged and an aliquot of the supernatant was mixed with methanol (1 mL) and glacial acetic acid (50 mL) plus approximately 100 µg each of non-radiolabeled fluroxypyr MHE, fluroxypyr, and fluroxypyridinol standards (p. 16). An aliquot of the mixture was analyzed by reverse-phase HPLC (C18 column) with a mobile phase gradient of (Solvent A) acetonitrile:methanol (50:50, v:v) and (Solvent B) distilled, deionized water, both with 1% acetic acid (A:B: 20:80 to 25:75 to 100:0, v:v); both UV (254 nm) and radioactive flow detection were used (pp. 20, 21). The method detection limit for HPLC analysis of water samples was 0.04 ng per 0.5-mL fraction (p. 22). Eluent fractions were collected and analyzed by LSC.

In a method validation study (raw data not reported) for the analysis of water samples, HPLC recoveries of radioactivity from samples fortified with [14C-2,6] fluroxypyr MHE and analyzed 30 minutes and 24 hours posttreatment were 67% and 65% of the applied, respectively (p. 17). Respective recoveries following LSC analysis were 86% and 89% of the applied. The study authors assumed the material loss during HPLC analysis to be the result of adsorption of the parent compound to syringe or injector surfaces. Because it was also assumed that the losses were not attributed to the main degradate (fluroxypyr), only parent compound recoveries were corrected (based on LSC recoveries versus HPLC recoveries) to account for material lost through adsorption (see Comment #1).

Four of the fish removed from the exposure tank at each sampling interval were solubilized in Soluene-350 and analyzed for total radioactivity by LSC; data were corrected for quenching and counting efficiency (p. 18). The remaining four fish were dissected into edible (muscle fillets) and nonedible portions (head, skin, viscera and

skeleton) prior to solubilization and LSC analysis. Both whole fish and inedible tissues were each sectioned into quarters prior to solubilization; reported data represent total radioactivity detected in the respective segments (four segments for each of four replicate samples) divided by the total weight of the tissues for all four samples. The method detection limits for LSC analysis of solubilized edible, nonedible and whole fish tissues were 0.3 ng/g, 0.3 ng/g and 0.4 ng/g, respectively (pp. 22, 23). Total radioactivity in whole fish tissues or separated tissue portions of control fish were determined using only one replicate for each sampling interval. To characterize radioactivity in fish tissues, additional fish sampled at 16 and 28 days posttreatment were dissected into edible and nonedible portions or left whole, and frozen (temperature unspecified). Tissue samples were homogenized (method not specified) while frozen and extracted three times with methanol containing 0.1% acetic acid. The combined extracts were concentrated, redissolved in methanol:acidified (0.5% phosphoric acid) water (50:50, v:v) and analyzed by LSC for total radioactivity (p. 19). Aliquots of the extracts were analyzed by HPLC (within one week of collection) as described previously for the water samples; the method detection limit was 0.05 ng per 0.5-mL fraction (p. 22). Nonextracted [14C]residues in tissue samples were quantified by solubilizing the post-extracted tissues followed by LSC analysis. Selected extracts from pooled day-28 samples (4 samples of 20 fish each) were isolated from methanol extracts by partitioning with chloroform and separated using HPLC; collected radioactive fractions were analyzed by GC/MS to confirm compound identities (p. 21).

In a method validation study (raw data not reported) for the analysis of fish tissue samples, mean extraction efficiencies from muscle and viscera tissue samples fortified with pyridine ring-labeled [14C-2,6]fluroxypyr MHE and the metabolite [14C]fluroxypyr were 95.8% and 93.6% of the applied, respectively; mean HPLC recoveries of radioactivity were 95.7% and 94.1% of the applied, respectively (p. 20). Total radioactivity recoveries by LSC from muscle and viscera tissue samples were 105.3% and 102.2% of the applied (p. 19).

To determine the frozen storage stability of the pesticide in fish tissues, a single replicate of whole fish extract sample (day 10) was analyzed by LSC immediately following preparation and was reanalyzed following 60 days of frozen storage (approximately -10 °C). Recovery of total radioactivity following frozen storage was 94% of that recovered initially (p. 34). Residue characterization of the whole fish extract by HPLC following storage indicated that relative concentrations of parent compound and the degradate fluroxypyr were similar to those observed in the unstored extract (p. 34).

#### DATA SUMMARY

Radiolabeled residues accumulated in rainbow trout that were exposed to pyridine ringlabeled [14C-2,6] fluroxypyr MHE (radiochemical purity 98.5%) at a nominal

concentration of 1.5 ng/mL under flow-through aquarium conditions. The actual mean concentration of the parent compound was reported (p. 27) as approximately 0.3 ng/mL (with the remaining radioactivity attributed to the degradate fluroxypyr); however, the analytical method of determining the parent compound aqueous concentration was questionable. Mean total [ $^{14}$ C]residues (reported as fluroxypyr MHE equivalents) were highest in the nonedible tissues ( $58.6 \pm 19.4$  ng/g) compared with edible ( $6.0 \pm 2.7$  ng/g) and whole fish tissues ( $52.4 \pm 26.1$  ng/g; Table 7, p. 45). Maximum mean concentrations of total [ $^{14}$ C]residues occurred on day 21 for each tissue type; mean radioactivity was a maximum concentration of 9.4 ng/g in edible tissues, 83.6 ng/g in nonedible tissues and 96.4 ng/g in whole fish tissues (Table 7, p. 45). Concentrations of [ $^{14}$ C]residues were variable with time, however, exhibiting a decrease in concentration from day 1 to day 10, followed by an increase in concentration up to day 21, with a rapid decrease observed by day 25 in both nonedible and whole fish tissues; in edible tissues, a similar pattern was seen from day 3 onward. The only major degradate observed in each tissue type was confirmed by GC/MS as the hydrolysis product

4-amino-3,5-dichloro-6-fluoro-pyridyloxyacetic acid (fluroxypyr, acid equivalent).

Complete residue concentration data for [14C-2,6] fluroxypyr and its degradates were not reported. At day 28, 1.4% (0.2 ng/g) and 91.9% (10.1 ng/g) of the radioactivity recovered from edible tissue samples was present as [14C-2,6] fluroxypyr MHE and fluroxypyr, respectively; for nonedible tissue samples, respective values were 5.1% (1.8 ng/g) and 83.7% (29.8 ng/g; Table 9, p. 47). Maximum bioconcentration factors (BCF; calculated by the reviewer as described in Comment #3) based on total radioactivity (including radiolabeled fluroxypyr MHE and fluroxypyr) were 6.06x for edible (muscle), 53.87x for nonedible (head, skin, viscera and skeleton) and 62.11x for whole fish tissues. Depuration was rapid, with the accumulated [14C] residues eliminated from the edible fish tissues by day 3 and from the whole fish tissues by day 7 (Table 7, p. 45). Accumulated [14C] residues were not observed in nonedible tissue at day 7, but were detected at 2.4, 6.8 and 1.3 ng/g on depuration days 10, 14 and 17, respectively.

The concentration of [14C]residues (in fluroxypyr MHE equivalents) in the water during the exposure period ranged from 1.17 to 1.95 ng/mL, with a mean of 1.53 ng/mL; no radioactivity was detected in (day 1 through 4) water samples during the depuration period (Table 4, p. 42). The only degradate detected in exposure water samples was the hydrolysis product fluroxypyr (acid). Residue characterization analysis of selected samples indicated that the majority (mean of 80%) of radioactive residues detected in aquarium water was present as the degradate fluroxypyr (Table 5, p. 43). The measured concentration of [14C-2,6]fluroxypyr MHE in the water at each sampling interval was questionable, however, due to the presumed adsorption of the compound to the syringe and injector (used in HPLC analysis) and the subsequent adjustment of parent compound values as described previously in the methods as well as in Comment #1 below.

Throughout the 28-day exposure and 17-day depuration period, the temperature of the water ranged from 12.0 to 13.7 °C, the pH ranged from 7.42 to 7.94, and the dissolved oxygen content ranged from 7.55 to 10.01 mg/L (Table 3, p. 41).

### **COMMENTS**

In a method validation study using water samples fortified with pyridine ring-labeled [14C-2,6] fluroxypyr MHE, radioactivity recoveries using LSC analysis were 86% and 89% of the applied for samples analyzed at 30 minutes and 24 hours posttreatment, respectively. Respective HPLC recoveries were 67% and 65% of the applied, respectively. The study authors assumed, based on relative water solubilities of the parent compound and the major degradate fluroxypyr, that the material loss during HPLC analysis was the result of adsorption of the parent compound (as opposed to the hydrolysis product, fluroxypyr) to syringe or injector surfaces. Based on this conclusion, total radioactivity and parent compound aqueous concentration data were adjusted or corrected by the study authors (based on differences in LSC recoveries versus HPLC recoveries) to account for material lost through adsorption (p. 17).

It is the conclusion of the reviewer that the analytical method was inappropriate for the quantification of the parent compound in water samples. It is also noted that, despite the rapid depuration observed, no [14C]residues were detected in depuration water samples; it is unclear whether this may have resulted from the inadequacy of the analytical method. Adequate gas chromatography (GC) methods were demonstrated in a fluroxypyr terrestrial field dissipation study (MRID 44080347) submitted by the registrant. It is suggested that this method be modified to facilitate the analysis of fluroxypyr MHE residues in water samples.

- 2. Complete tissue concentration data (for the parent compound, the major degradate and any minor degradates) were not reported for each tissue type and sampling interval; instead, values (for the parent compound and the major degradate only) were reported for selected tissue types at selected intervals (Table 9, p. 47). Although large samples of fish were removed at day 28 for the purpose of metabolite identification, residue concentration data were reported only for the edible and nonedible tissues for this sampling interval. No minor metabolites were identified, although the study authors noted (in footnote "a" of Table 9) that not all of the applied (and recovered) radioactivity detected in fish tissue samples was accounted for by the parent compound and the single major degradate.
- Bioconcentration factors for edible, nonedible; and whole fish tissues were calculated by the reviewer by dividing the mean measured concentration of [14C]residues in the fish tissues at each sampling interval (Table 7) by the mean measured water concentration up to and including the respective sampling day (calculated by reviewer based on data

reported in Table 4). This method enabled the reviewer to determine the maximum mean bioconcentration factors. In contrast, the study authors calculated BCF's using a SimuSolv computer modeling program. Using a two-compartment model, total radioactivity BCF values of 21x, 217x and 167x were determined for edible, nonedible and whole fish tissues, respectively (Table 8, p. 46). Using a four-compartment model which accounted for parent compound plus metabolites (fluroxypyr acid here), respective BCF values for fluroxypyr MHE were determined to be 0.6x, 25x and 26x for edible, nonedible and whole fish tissues (Table 10, p. 48).

- 4. Concentrations of [14C]residues in fish tissues were variable with time for each tissue type and did not exhibit definite plateaus, but decreased (after a first "peak" at day 1 or day 3) and then increased to a maximum, followed by a rapid decrease. The study authors stated that the observed variability in tissue concentrations, which precluded the determination of a plateau, may have been the result of an inconsistent parent compound exposure concentration (p. 29). The reviewer considers this a likely explanation based on the aqueous concentration of parent compound as displayed in Figure 7 (p. 56) and the tissue accumulation patterns displayed in Figures 8, 9 and 10 (top graph in each; pp. 57-59). Thus, tissue accumulation was dependent on the concentration of parent compound in the test water, rather than on the total radioactivity (from parent compound plus the degradate fluroxypyr) present.
- 5. As noted above, due to variability in tissue [14C]residue concentrations (assumed to result from variable parent compound aqueous concentrations) concentration plateaus in fish tissues could not be determined. The study authors stated that mean total radioactivity in fish tissues could be used as an estimate of the concentration plateau for each tissue type and, based on this method of determination, plateau levels were concluded to have occurred at day 1 for nonedible and whole fish tissues and at day 3 for edible tissues (p. 28). The reviewer does not concur with the study authors' conclusion that the estimated concentration plateaus are an acceptable substitute for observed plateaus.
- 6. A water solubility of approximately 115 ng/mL was reported for fluroxypyr MHE; however, the temperature at which the solubility was determined was not specified (p. 9). The reviewer notes that the reported water solubility of test compounds are generally determined at 20-25 °C, while this bioaccumulation study was performed at 12° C. The study authors noted that the water solubility of the degradate fluroxypyr acid was 91 mg/L at 20° C and that this was significantly greater than the water solubility of the parent compound (p. 17). The water solubility of fluroxypyr acid was reportedly 7.95± 0.04 g/L at pH 7.5 (MRID# 44080349).
- 7. Based on the results of previous acute studies with rainbow trout, the 96-hour LC<sub>50</sub> value for fluroxypyr MHE was determined to range from 3 to 13 mg/L (8 to 19 mg/L in one study) and the no-observed effect concentration was a range of 1.0-1.8 mg/L (p. 11). In a separate study, rainbow trout and golden orfe showed no mortality or sublethal effects

15,

when exposed to fluroxypyr MHE at concentrations ranging from 0.18 to 5 mg/L (p. 11). Based on these results, an exposure concentration of 1.5  $\mu$ g/L (approximately 0.03% of 5 mg/L) was chosen for the study reviewed here.

- 8. The study authors stated that mortality rates of 1.3% and 0.3% were observed in the exposure and control tanks, respectively, during the uptake phase of the study (p. 15).
- 9. Rainbow trout were used to study the bioaccumulation of fluroxypyr MHE in a laboratory setting; it is recommended that either bluegill sunfish or channel catfish be used.
- 10. The frozen storage temperature was not reported in the methods section of the study. However, the study authors noted that the single sample analyzed to determine the storage stability of the pesticide in whole fish tissues was stored at -10° C.
- 11. The study authors stated that the fraction of total radioactivity in the mixing chamber water attributed to the parent compound was observed to be relatively low (44%) at exposure day 15 (27). The chamber was removed at that point, cleaned and reinstalled. The study authors stated that, as depicted in Figure 6, a follow-up analysis of the mixing chamber water indicated a "marked increase in the fluroxypyr MHE composition compared to the day 15 analysis."

## DATA EVALUATION RECORD ALGAE OR DIATOM EC<sub>50</sub> TEST **GUIDELINE 123-2 (TIER II)**

PC Code No.: 128959 1. CHEMICAL: Fluroxypyr

2. TEST MATERIAL: 4-amino-3,5-dichloro-6-fluro-2-methoxypyridine

(a metabolite of fluroxypyr)

Purity: 99.9%

3. CITATION

H. D. Kirk and A. M. Landre Authors:

Title: Evaluation of the phytotoxicity of 4-amino-3,5-dichloro-6-

fluro-2-methoxypyridine to green algae, Selenastrum

.capricornutum Printz

Study Completion Date:

October 6, 1995

Laboratory:

The Environmental Toxicology & Chemistry Research

Laboratory, Dow Chemical Company

Sponsor:

DowElanco

Laboratory Report ID: DECO-ES-3029

DP Barcode:

D231718

MRID No.:

440803-41

4. REVIEWED BY: F. Nicholas Mastrota, Wildlife Bioilogist, ERB II, EFED

F. Nicholas Mastrota

Date: 10/7/97

5. PEER REVIEW BY: Andrew Bryceland, Fishery Bioilogist, ERB II, EFED

Signature:

10/7/57

6. STUDY PARAMETERS

Definitive Test Duration:

120 hours

Type of Concentrations:

Nominal

7. <u>CONCLUSIONS</u>: The concentration of 4-amino-3,5-dichloro-6-fluro-2-methoxypyridine (a metabolite of fluroxypyr) that is predicted to cause 50% inhibition of population growth of Selnastrum capricornutum is 2.4 ppm ai. Concentrations of 0.94 ppm or less caused no observed effect on cell density.

Results Synopsis

EC<sub>50</sub>: 2.4 ppm ai

95% C.I.: 1.8-3.2 ppm ai

NOEL: 0.938 ppm ai

Slope: 2.82

### 8. ADEQUACY OF THE STUDY

A. Classification: Supplemental.

**B.** Rationale: The study was not conducted in compliance with FIFRA Good Laboratory Practices.

C. Repairability: Not repairable.

### 9. GUIDELINE DEVIATIONS

- 1. The study was not performed according to the FIFRA Good Laboratory Practices, although the report states that the study "followed the basic principles of Good Laboratory Practices".
- 2. The progression of doses was 4X, whereas a 2X or 3X progression is recommended.
- 3. The study report did not mention if daily observations were made.
- 10. SUBMISSION PURPOSE: Section 3 registration of Fluroxypyr MHE

### 11. MATERIALS AND METHODS

### A. Test Organisms

Guideline Criteria	Reported Information
Species Skeletonema costatum Anabaena flos-aquae Selenastrum capricornutum Navicula pelliculosa	Selenastrum capricornutum
Initial Number of Cells 3,000 - 10,000 cells/ml	~ 10,000 cells/ml
Nutrients Standard formula, e.g. 20XAAP	Algal assay medium (AAM)

### B. Test System

Guideline Criteria	Reported Information
Solvent	Acetone (≤0.1 ml/L)

DP Barcode: D231718 ' MRID No.: 440803-41

Güdeline Criteria	Reported Information
Temperature Skeletonema: 20°C Others: 24-25°C	24±2°C
Light Intensity Anabaena: 2.2 K lux (±15%) Others: 4.3 K lux (±15%)	4.3 K lux
Photoperiod Skeletonema: 14 h light, 10 h dark or 16 h light, 8 h dark Others: Continuous	Continuous
pH Skeletonema: approx. 8.0 Others: approx. 7.5	7.2-8.1

# C. Test Design

6.711. 6.32.3	D 311.6
Guideline Criteria	Reported Information
Dose range	
2X or 3X progression	4X .
<u>Doses</u>	
at least 5	6
Controls	
negative and/or solvent	Negative and solvent controls were used.
Replicates per dose	
3 or more (4 or more for Navicula)	3
Duration of test	
120 hours	120 hours
Daily observations were made?	Not reported
Method of Observations	Cellular counts
Maximum Labeled Rate	For parent compound:
	1.5 lb ae/acre

DP Barcode: D231718 MRID No.: 440803-41

# 12. REPORTED RESULTS

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	No. There was a quality insurance statement, but the study did not comply with GLP.
Initial and 120 h cell densities were measured?	Yes
Control cell count at 120 hr ≥2X initial count?	Yes
Initial chemical concentrations measured? (Optional)	No
Raw data included?	Yes

Dose Response

Dose (mg:ai/L)	Cell Density (x 10 <sup>4</sup> cells/ml)	% Inhibition	120-Hour pH
Media Control	203.1		8.1
Solvent Control	210.4		8.3
0.015	243.8	-17.9	8.3
0.059	240.2	-16.2	8.5
0.234	218.0	-5.42	8.4
0.938	180.2	12.9	8.4
3.80	69.41	66.4	7.5
15.0	1.404	99.3	7.2

Other Significant Results: None.

DP Barcode: D231718 ' MRID No.: 440803-41

## Statistical Results:

Statistical Method: Linear regression of log concentration versus cell counts, Dunnett's test

EC<sub>50</sub>: 2.164 ppm

95% C.I.: Not reported

Slope: Not reported

NOEC: 0.938 ppm

## 13. Verification of Statistical Results

Statistical Method: Nonlinear regression (Bruce and Versteeg, 1992), Williams test

EC<sub>50</sub>: 2.4 ppm ai

95% C.I.: 1.8-3.2 ppm ai

Slope: 2.82

NOEC: 0.938 ppm ai

## 14. REVIEWER'S COMMENTS: None.

308/2E March 31, 1998



Document Processing Desk 6(a)(2)
Office of Pesticide Programs (7504C)
U. S. Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Attention: Ms. Joanne I. Miller/PM-23 (7505C)

STARANE F (EPA FILE SYMBOL: 62719-EIL) A.I.: FLUROXYPYR METHYLHEPTYL ESTER (MHE)

STARANE EC (EPA FILE SYMBOL: 62719-EIA)

EPA PETITION NO. 6F4772

RESPONSE TO DATA EVALUATION RECORDS CONCERNING THE REVIEW OF ECOLOGICAL STUDIES SUBMITTED IN THE FLUROXYPYR APPLICATION FOR PESTICIDE REGISTRATION DATED AUGUST 6. 1996

On October 7, 1998, we received your letter dated October 1, 1997 (including memorandums dated July 28, 1997 and July 30, 1997). This review contained a number of Data Evaluation Records (DERs) for the ecotoxicological evaluation of fluroxypyr methylheptyl ester, the active ingredient in Starane\* F herbicide and Starane EC herbicide. The memorandum dated July 28, 1997 addressed MRIDs 44080308 through 44080313 and MRID 44080339. The memorandum dated July 30, 1997 addressed MRIDs 44080314, 44080335 through 44080338. and 44080340. While most of the ecological effects data were found to be acceptable, three studies were not; these included:

- Aquatic plant study on the freshwater diatom, Navicula pelliculosa (MRID #44080339)
   Classified: Invalid (repairable) on review dated July 28, 1997
   Fluroxypyr 1-Methylheptyl Ester: The Toxicity to the Freshwater Diatom, Navicula pelliculosa
   Study ID: ES-3075, Author: Milazzo, D.P. et. al, Study Completion Date: June 4, 1996
- Estuarine/marine study examining the shell deposition effects with the Eastern oyster
   (MRID #44080310) Classified: Supplemental (not repairable) on the review dated July 28, 1997
   Fluroxypyr 1-Methylheptyl Ester: Acute Flow-Through Mollusc Shell Deposition Test
   Study ID: 646-DO (DECO-ES-2625), Author: Boeri, R.L. et. al, Study Completion Date: January 12, 1996
- Chronic toxicity of fluroxypyr MHE to the daphnid Daphnia magna Straus (MRID #44080314)
   Classified: Supplemental (may be upgraded) on review dated July 30, 1997
   Evaluation of the Chronic Toxicity of Fluroxypyr 1-Methylheptyl Ester to the Daphnid, Daphnia magna STRAUS. Study ID: DECO-ES-3079, Kirk, H.D. et.al, Study Completion Date: July 15, 1996

In the enclosed attachment, I am forwarding a response from our Environmental Sciences Laboratory, in the form of a letter addressed to me, that addresses the concerns brought forward in these DERs. This response contains additional information to support the above studies so that they may be judged acceptable. The aquatic plant study on the freshwater diatom, Navicula pelliculosa (MRID 44080339) has been upgraded and is being submitted as supplemental data.



Trademark of Dow AgroSciences LLC

Ms. Joanne I. Miller/PM-23 (7505C)

STARANE F.(EPA FILE SYMBOL: 62719-EIL) A.I.: FLUROXYPYR METHYLHEPTYL ESTER (MHE)

STARANE EC (EPA FILE SYMBOL: 62719-EIA)

**EPA PETITION NO. 6F4772** 

RESPONSE TO DATA EVALUATION RECORDS CONCERNING THE REVIEW OF ECOLOGICAL STUDIES SUBMITTED IN THE FLUROXYPYR APPLICATION FOR PESTICIDE REGISTRATION DATED AUGUST 6, 1996

March 31, 1998

Page 2

#### Contents of Submission

Volume/Guidelines MRID NO. Contents/Study

Volume 1

(Administrative)

Transmittal document (this letter)

General Summary for Public Release (1)

Complimentary Copy: Letter from Kent B. Woodburn, Ph.D. (The Dow Chemical Company) to John J. Jachetta (Dow AgroSciences) dated 3/4/98

Pages 1-14

Complimentary Copy: EPA letter dated 10/1/97

Complimentary Copy: EPA Memorandum dated 7/28/97
Complimentary Copy: EPA Memorandum dated 7/30/97.
Complimentary Copy: DER on MRID 44080339 dated 6/26/97
Complimentary Copy: DER on MRID 44080310 dated 7/28/97
Complimentary Copy: DER on MRID 44080314 dated 7/25/97

Volume 2

123-2

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6(a)(2)

consideration

SUPPLEMENTAL REPORT FOR: FLUROXYPYR 1-METHYLHEPTYL ESTER: THE TOXICITY TO THE FRESHWATER DIATOM. Navicula

. pelliculosa

Kirk, H.D. et al.

March 17, 1998

Study ID: ES-3075

Pages: 1-44

(3 copies)

Thank you for your consideration of this additional information. If you have other questions or concerns regarding these, or any studies, please contact me at (317) 337-4672 or Joyce Armstrong, Registration Assistant for this product, at (317) 337-4657.

Sincerely,

John J. Jachetta, Ph.D. Regulatory Manager

Regulatory Success - Americas

(317) 337-4649 (FAX)

JJJ/ila/ls

Enclosures

# U.S. ENVIRONMENTAL PROTECTION AGENCY Office of Pesticide Programs

DOW AGROSCIENCES LLC 9330 ZIONSVILLE ROAD 308/3E INDIANAPOLIS, IN 462681054

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 04/01/98. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal has not been analyzed for compliance with PR Notice 86-5, due to the fact that it was submitted under the requirements of FIFRA Section 6(a)2. A copy of your transmittal letter is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted.

308/2E January 19, 1998



Document Processing Desk
Office of Pesticide Programs (7504C)
U.S. Environmental Protection Agency
Room 266A Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Attention: Joanne I. Miller/PM-23 (7505C)

FLUROXYPYR: PP#6F4772

EPA FILE SYMBOL NUMBER: STARANE\* F (62719-EIL) EPA FILE SYMBOL NUMBER: STARANE EC (62719-EIA) DATA SUBMISSION - PUBLIC INTEREST DOCUMENT

A Public Interest Document (PID) is being provided to the Agency supporting the registration of Fluroxypyr (Starane\*) to control herbicide-resistant *kochia* and volunteer potato in cereal grains. This assessment provides background on the specific benefits of fluroxypyr and reviews use rates, application methods, and availability of alternative (herbicides and non-chemical control methods).

#### Contents of Submission

<u>Volume</u>	MRID NO.	Contents/Study	
Volume l (Administrative)	<b>~</b>	Transmittal document (this l General Summaries for Pub	•
Volume 2 (N/A)	44464801	Public Interest Document St of Fluroxypyr (Starane*) to Kochia and Volunteer Potate Nelson, J.E., et al. Study ID: PID-10352 Pages: 1-65	Control Herbicide-Resistant

10%

<sup>\*</sup> Trademark of Dow AgroSciences LLC

Joanne I. Miller/PM-23 (7505C) FLUROXYPYR: PP#6F4772

EPA FILE SYMBOL NUMBER: STARANE\* F (62719-EIL) EPA FILE SYMBOL NUMBER: STARANE EC (62719-EIA) DATA SUBMISSION - PUBLIC INTEREST DOCUMENT

January 19, 1998

Page 2

If you require further information, please contact me at (317) 337-4672, or Joyce Armstrong, Registration Assistant for this product, at (317) 337-4657.

Sincerely,

John J. Jachetta, Ph.D.

Regulatory Manager

Regulatory Success Americas

(317) 337-4649 (FAX)

JJJ/jla/ls

Enclosures

cc: Bruce Riggle, Registration Manager United Agri Products 419 18<sup>th</sup> St., P.O. Box 1286 Greeley, Colorado 80632

# U.S. ENVIRONMENTAL PROTECTION AGENCY Office of Pesticide Programs

DOW AGROSCIENCES LLC 9330 ZIONSVILLE ROAD 308/3E INDIANAPOLIS, IN 462681054

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 01/22/98. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

Dow AgroSciences FLC 9330 Zionsville Road Indianapolis, IN 46268-1054 I talked to John

Jacketta. He will send in

3 copies of the entire

study (with corrected page

for our files. Joanne

Dow AgroSciences

308/2E January 9, 1998

Document Processing Desk
Office of Pesticide Programs (7504C)
U.S. Environmental Protection Agency
Room 266A Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Attention: Joanne I. Miller/PM-23 (7505C)

FLUROXYPYR: PP#6F4772

EPA FILE SYMBOL NUMBER: STARANE\* F (62719-EIL) EPA FILE SYMBOL NUMBER: STARANE EC (62719-EIA)

REVISION TO DATA FORMAT DEFICIENCY ON SUBMISSION DATED AUGUST 6, 1996

Enclosed please find three copies of a replacement page (18R) for your current page 18 of study number K-129976-012 (MRID 44080321). This study was originally submitted August 6, 1996 on the Application for New Registration - Section 3, with the Petition for Permanent Tolerance for Fluroxypyr Methylheptyl Ester (MHE) Residues on Wheat, Barley and Oats.

The EPA Data Review from Linda Taylor dated September 25, 1997 listed this study as acceptable. However, it was noted on page 11 of the review that the CAS No. referred to in the study was incorrectly reported as 81406-37-3.

We are enclosing a Complimentary Copy of a letter sent to me from T. K. Jeffries of The Dow Chemical Company explaining the actions taken to correct the CAS number on this study to read CAS No. 69377-81-7.

<u>Correction</u>	Volume No.	Stud	<u>.</u>
Revised Page 18R	Volume 23 (83-4) 6(a)(2) consideration	Fluroxypyr: Two Generation E Toxicity Study in Sprague-Daw	•
		Vedula, U. <i>et.al</i> Study ID: K-129976-012	June 19, 1996 (3 copies of replacement page)

If you require further information, please contact me at (317) 337-4672, or Joyce Armstrong, Registration Assistant for this product, at (317) 337-4657.

John J. Jachetta, Ph.D.

Regulatory Manager
U.S. Regulatory, Toxicology and
Environmental Chemistry
(317) 337-4649 (FAX)

JJJ/jla/ls

**Enclosures** 

Sincerely,

<sup>\*</sup> Trademark of Dow AgroSciences LLC

## Statement of GLP Practice.

This study was conducted in accordance with the Environmental Protection Agency (EPA); FIFRA Good Laboratory Practice Standards (Final Rule), OECD Principles for Good Laboratory Practice, EEC Good Laboratory Practice Standards as cited in European Economic Community (EEC) Directive 87/18/EEC, the Japanese Ministry of Agriculture, Forestry and Fisheries Good Laboratory Practice Standards and the Standard Operating Procedures of The Toxicology Research Laboratory of The Dow Chemical Company.

In addition, in response to the Final Rules amending the U.S. Animal Welfare Act that were promulgated by the U.S. Department of Agriculture effective October 30, 1989, the Animal Care and Use Activity (ACUA) that was required for the conduct of this study was reviewed and given full approval by the Institutional Animal Care and Use Committee (IACUC).

### MATERIALS AND METHODS

Test Material:

Fluroxypyr

Supplier (Lot #):

DowElanco (AGR 295035)

Synonyms:

DOWCO\* 433

Chemical Name:

((4-amino-3, 5 dichloro-6-fluoro-2-pyridinyl)

oxy) acetic acid.

CAS Number:

69377-81-7

Molecular Formula:

 $C_7 H_5 Cl_2 F N_2 O_3$ 

Structural Formula:

The test material was characterized by Liang (1991) using the following methods: structure confirmation & impurity determination by nuclear

<sup>\*</sup>Trademark of The Dow Chemical Company

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Trademark of The Dow Chemical Company

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Structural Formula:

The test material was characterized by Liang (1991) using the following methods: structure confirmation & impurity determination by nuclear

<sup>\*</sup> Trademark of The Dow Chemical Company

The Dow Chemical Company Midland, Michigan 48674

John J. Jachetta, Ph.D. Registration Manager DowElanco 9330 Zionsville Road Indianapolis, IN 46268-1054

## COMPLIMENTARY COPY

## RESPONSE TO FLUROXYPYR TOXICOLOGY DATA EVALUATIONS

Dear Dr. Jachetta,

I have verified that the CAS numbers for Fluroxypyr (also known as Fluroxypyr acid) is 69377-81-7 and the CAS number for Fluroxypyr 1-methylheptyl ester (also known as Fluroxypyr methylheptyl ester) is 81406-37-3. The following table lists the 6 studies described on page 11 of the EPA letter from Linda Taylor (25 September 1997), Subject: Data Reviews, the correct CAS number, and the CAS number that was reported. As you can see, the CAS number for the 2-generation reproduction study was the only CAS number that was reported incorrectly.

Study	Test Material	Correct CAS	Reported CAS
metabolism	Fluroxypyr	69377-81-7	69377-81-7
90-day rat	Fluroxypyr	69377-81-7	69377-81-7
2-gen reproduction	Fluroxypyr	69377-81-7	81406-37-3
metabolism	Fluroxypyr methylheptyl ester	81406-37-3	81406-37-3
mutagenicity	Fluroxypyr methylheptyl ester	81406-37-3	81406-37-3
rat developmental	Fluroxypyr 1-methylheptyl ester	81406-37-3	81406-37-3

I will initiate a Report Change/Revision for the 2-generation reproduction report to correct this error. If I can help in any other way, please feel free to contact me.

Sincerely,

T.K. Jeffries

The Dow Chemical Company

1803 Building

Midland, Michigan 48674

(517) 636-6860

K



# UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND TOXIC SUBSTANCES

### **MEMORANDUM**

DATE:

December 23, 1997

TO:

Daniel Kenny

Herbicide Branch - PM23

Registration Division (7505C)

FROM:

William R. Effland, Ph.D.

Mille

ffland 12/23/97

Environmental Scientist

Environmental Risk Branch II

Environmental Fate and Effects Division (7507C)

THROUGH:

Elizabeth M.K. Leovey, Ph.D.

Branch Chief EFED/ERB II

RE:

Drinking Water Screening Exposure Assessment for Fluroxypyr

(PC Code: 128959; DP Barcode: 241115)

### **SUMMARY**

This memorandum describes the water resources screening assessment for fluroxypyr "acid" (4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetic acid) formulated as fluroxypyr-1-methylheptyl ester (fluroxypyr-MHE). In terrestrial and aquatic environments, fluroxypyr-MHE is rapidly hydrolyzed to fluroxypyr acid which has herbicidal activity. Fluroxypyr acid is further degraded (although less rapidly) via microbial-mediated metabolism to 4-amino-3,5-dichloro-6-fluoro-pyridin-2-ol ("pyridinol" degradate) and 4-amino-3,5-dichloro-6-fluoro-2-methoxypyridine ("methoxypyridine" degradate). In aerobic environments, fluroxypyr acid and the pyridinol and methoxypyridine degradates are ultimately metabolized to carbon dioxide (totaled 46.8-76.2% of the applied radioactivity in the aerobic soil study).

The assessment discusses the screening modeling results for both surface water and ground water media and includes an Environmental Fate Assessment for fluroxypyr. Water resource monitoring data are not available for fluroxypyr-MHE or fluroxypyr acid. Data reported in Table

1 presents the maximum acute and chronic surface water concentrations estimated from GENEEC Version 1.2 modeling. For surface water resources, the maximum acute estimated environmental concentration (EEC) was 11.2  $\mu$ g/L and the maximum chronic EEC was 3.9  $\mu$ g/L when fluroxypyr was modeled at 0.25 lbs acid equivalents/A/yr using aerial application. Results of the Groundwater Screening Assessment using SCI-GROW2 estimated the acute and chronic EEC for groundwater to be 0.025  $\mu$ g/L. The modeling inputs are shown in Tables 2 and 3.

Table 1. Surface Water EECs (µg/L) using GENEEC Version 1.2

Maximum EEC	Mean 4-Day EEC	Mean 21-Day EEC	Mean 56-Day EEC
11.2	10.4	7.1	3.9

#### **Environmental Fate Assessment**

Degradation of fluroxypyr-MHE in environmental fate laboratory studies occurs through base-catalyzed hydrolysis and microbial-mediated metabolism under aerobic conditions. In sterilized buffered water, fluroxypyr-MHE hydrolyzed to the fluroxypyr acid with half-lives of 3 and 454 days at pH 9 and 7, respectively. Hydrolysis of fluroxypyr-MHE was not observed in the acidic test system at pH 5. In the aerobic soil metabolism study, microbial degradation of fluroxypyr-MHE appears to follow a biphasic degradation pattern with an initial first-order half-life of 1 to 3 weeks in four soils. The rate of metabolism decreased significantly after 2 months. Degradation of fluroxypyr-MHE yields fluroxypyr acid (the herbicidal agent), 4-amino-3,5-dichloro-6-fluoro-pyridin-2-ol (pyridinol metabolite), 4-amino-3,5-dichloro-6-fluoro-2-methoxypyridine (methoxypyridine metabolite) and CO<sub>2</sub>. The aerobic aquatic metabolism half-life was estimated to be 14 days.

Fluroxypyr acid is considered mobile based on Freundlich  $K_{ads}$  values ranging from 0.11-1.9 ml/g in four test soils (silt loam, sandy loam, loam, and silty clay textures). These soil/water partitioning coefficients indicate fluroxypyr will occur principally in the aqueous phase of soil/water systems.

Table 2. Ground Water Exposure Assessment using SCI-GROW2

MODEL INPUT VARIABLE	INPUT VALUE
Application Rate (lbs. ai/A)	0.25
Maximum No. of Applications	1
Koc	68 (median; n = 4)
Aerobic Soil Metabolic Half-life (days)	14 (mean; n = 4)

Table 3. Surface Water Exposure Assessment using GENEEC (v.1.2)

MODEL INPUT VARIABLE	INPUT VALUE
Application Rate (lbs ai/A)	0.25
Maximum No. of Applications	.1
Koc	50 (minimum reported value)
Aerobic Soil Metabolic Half-life (days)	23 (maximum of 4 reported values)
Is the pesticide wetted-in?	No .
Depth of Incorporation (in.)	0.0
Spray Drift	Aerial (5%)
Solubility (mg/L)	0.90
Aerobic Aquatic Metabolic Half-life (days)	14
pH 7 Hydrolysis Half-life (days)	stable (454 days)
Photolysis Half-life (days)	0 (stable )

Robert F. Bischoff DowElanco 9330 Zionsville Road Indianapolis, IN 46268

OCT | 1997

Dear Mr. Bischoff:

Subject: ·

Fluroxypyr - Application for Pesticide Registration

Starane F (EPA File Symbol 62719-EIL) Starane EC (EPA File Symbol 62719-EIA)

EPA Petition No. 6F4772

Your Submission Dated August 6, 1996

The Agency has completed an additional review of the application for pesticide registration referenced above. The following comments apply regarding the toxicology data provided with this application:

Although most of the toxicology studies submitted in support of this application were found to be acceptable, the mammalian cell gene mutation assay (MRID #440083-24, §84-2) was classified as unacceptable. The study may be upgraded with the submission of additional information as described in the enclosed review.

A complete copy of the review is included with this letter to provide the details of the review and the reasoning behind the above decision. You will be notified upon the completion of the remaining reviews.

Sincerely yours,

Joanne I. Miller Product Manager (23) Herbicide Branch Registration Division (7505C)

Enclosure

DK:305-7546:HB/PM23 CONCURRENCES									
SYMBOL .	7505C								
SURNAME .	DKENNY								
DATE -	10/1/97							1	



## UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

Jay C 9/25/97

**MEMORANDUM** 

SUBJECT:

FLUROXYPYR and FLUROXYPYR METHYLHEPTYL ESTER: Data

Reviews

FROM:

Linda L. Taylor, Ph.D.

Reregistration Branch I,

Toxicology Branch II, Section II [formerly]

Health Effects Division (7509C)

THRU:

Whang Phang, Ph.D.

Branch Senior Scientist

Reregistration Branch I

Health Effects Division (7509C)

TO:

Barbara Madden

**RCAB** 

Health Effects Division (7509C)

Registrant:

DowElanco

Chemical:

((4-amino-3,5-dichloro-6-fluoro-2-pyridinyl)

oxy) acetic acid

Synonym:

Fluroxypyr

Caswell No.:

463 O

P.C. Code:

128959

DP Barcode:

D232217/232550

Submission:

S515138

Action Requested: Please review the data and accompanying F petition

materials.

on Comment: studies submitted Fluroxypyr and Fluroxypyr The methylheptyl ester have been reviewed and the DERs are appended. There were no accompanying F petition materials.

In MRID 44080328, the Registrant provides a summary/review of the toxicology studies performed on Fluroxypyr and Fluroxypyr methylheptyl ester. In general, comparable toxicity is observed. Both compounds have been tested in rat and rabbit developmental toxicity studies, in rat subchronic-toxicity studies, and in mutagenicity studies.

[1] MRID 44080316 - In the subchronic oral toxicity study in rats, Fluroxypyr [98.9% a.i.] was administered to 10 Fischer 344 rats/ sex/dose via the diet at dose levels of 0, 320, 700, and 1000 mg/kg/day for 13 weeks. An additional 10 rats/sex/group were dosed at 0 and 1000 mg/kg/day for 13 weeks followed by a 4-week recovery period on basal

diet. There were no deaths, and no effects were observed on clinical. signs, ophthalmoscopy, urinalysis, gross or microscopic examinations in either sex. A slight decrease in body-weight gain was observed in both sexes at the high-dose level [overall gain od 95/99 94%% of control values], and the recovery-phase rats also displayed decreased bodyweight gains. Food consumption was not adversely affected by treatment. At the terminal sacrifice, slight increases in kidney weights were observed in both sexes at the high-dose level, but there were no microscopic lesions observed. Other organ-weight macroscopic or differences observed at the limit dose were decreased brain weight in females, increased liver weight in females, decreased testes weight in males, and increased kidney weight in males following the recovery phase. The LOEL is 1000 mg/kg/day, based on decreased body-weight gain in males, increased kidney weight in both sexes, and an apparent decrease in brain weight in females and testes weight in males. The NOEL is 700 mg/kg/day.

This guideline [§82-1] subchronic oral toxicity study in the rat is <a href="Acceptable"><u>Acceptable</u></a>.

[2] MRID 44080317 In the carcinogenicity study in mice, Fluroxypyr [98.92% a.i.] was administered to 60 CD-1 mice/sex/dose via the diet at dose levels of 0, 100, 300, and 1000 mg/kg/day for 18 months.

There were no adverse effects on survival or clinical signs in either sex. A slight decrease in body weight was observed in the high-dose males [93% of control value at study termination] and decreased bodyweight gains [overall gain of 80%/99 92% of control] were observed at the high-dose level in both sexes. Food consumption was not adversely affected by treatment. There were no adverse effects observed on any of the monitored hematology or ophthalmoscopy parameters in either sex. At the terminal sacrifice, there was a slight increase in the incidence of distended gall bladder (both macroscopically and microscopically) in both sexes at the high-dose level and a slight increase in the number of mice of both sexes with kidneys that were considered decreased in size. Organ weights, including the kidneys, were comparable among the groups in both sexes. Microscopically, there was a significant increase in the incidence of renal papillary necrosis and regenerative nephrosis [severe grade only] in the high-dose females. There was no apparent treatment-related increase in the incidence of any tumor type in either sex. The LOEL is 1000 mg/kg/day, based on decreased body weight/gain in males and an increased incidence of kidney lesions in females. The NOEL is 300 mg/kg/day.

This guideline [§83-2] carcinogenicity study in the mouse is Acceptable.

[3] MRID 44080318 - Under the conditions of this range-finding developmental toxicity study, the administration of Fluroxypyr methylheptyl ester [95.8% a.i.] to 10 naturally-mated female Sprague-Dawley CD $^{\odot}$  [SD] BR rats/group via gavage at dose levels of 0 [Mazola $^{\odot}$  corn oil], 100, 500, 750, and 1000 mg/kg/day from days 6 through 15 of gestation resulted in treatment-related increases in mortality at the two highest dose levels [40% and 70% at 750 and 1000 mg/kg/day,

respectively) and the termination of the highest dose group on day 11 of gestation. There were no treatment-related effects on clinical signs or gross pathologic alterations, body weight/gain, food consumption, absolute and relative liver and kidney weights at dose levels of 500 mg/kg/day and below. Decreased body-weight gain was observed at 750 mg/kg/day. Comparable pregnancy rates were observed among the groups [750 mg/kg/day and below], and there were no premature deliveries or dams with 100% intrauterine deaths. All dams had live fetuses at and there were comparable numbers of corpora necropsy, implantations, resorptions, and live fetuses among the groups. There were no treatment-related effects on reproductive parameters at dose levels up to 750 mg/kg/day. The results indicate that a dose of 750 mg/kg/day would be inappropriate for a definitive developmental toxicity study based on severe maternal toxicity [death]. The maternal NOEL in this range-finding study is 500 mg/kg/day, the LOEL is 750 mg/kg/day, based on deaths and decreased body-weight gain.

This non-guideline [§83-3(a)] prenatal developmental toxicity range-finding study in the rat is classified <u>Acceptable</u>.

[4] MRID 44080319 - Under the conditions of this developmental toxicity study, the administration of Fluroxypyr methylheptyl ester [95.8% a.i.] to 20 naturally-inseminated New Zealand female rabbits/group via gavage at dose levels of 0 [vehicle METHOCEL A4M], 100, 500, and 1000 mg/kg/day from days 7 through 19 of gestation resulted in maternal toxicity at the high-dose level, as evidenced by an increased incidence of abortions. Body weight was comparable among the groups, but body-weight gains were decreased at the mid- and high-dose levels [not doserelated] mainly during the dosing period, which may be attributed to palatability. Corrected maternal body weight was comparable among the groups. Comparable pregnancy rates were observed among the groups, and there were no premature deliveries or does with 100% intrauterine deaths. All does had live fetuses at necropsy, and there were comparable numbers of corpora lutea, implantations, resorptions, and live fetuses among the groups. Both pre- and post-implantation losses were comparable among the groups. Fetal body weight was slightly decreased [97% of control] at the high-dose level compared to the concurrent control, but this may be attributed to the increased number of fetuses per doe at this dose level. There were no external, skeletal, or visceral anomalies or variations that could be attributed to treatment, and there was no treatment-related increase in visceral or skeletal malformations. Although there was an apparent increase in the incidence of a minor anomaly, retrocaval ureter, at the mid- and high-dose levels, its toxicological significance is doubtful. The maternal/developmental LOEL is 1000 mg/kg/day, based on an increased incidence of abortions. The maternal NOEL is 500 mg/kg/day.

This guideline [§83-3(b)] prenatal developmental toxicity study in the rabbit is classified <u>Acceptable</u>.

[5] MRID 44080320 - Under the conditions of this range-finding developmental toxicity study, the administration of Fluroxypyr methylheptyl ester [95.8% a.i.] to 7 time-mated New Zealand female

rabbits/group via gavage at dose levels of 0 [vehicle METHOCEL A4M], 300, 500, 750, and 1000 mg/kg/day from days 7 through 19 of gestation resulted in no treatment-related effects on survival, clinical or gross pathologic alterations, body weight/gain, food consumption, absolute and relative liver and kidney weights. Comparable pregnancy rates were observed among the groups, and there were no premature deliveries or dams with 100% intrauterine deaths. All does had live fetuses at and there were comparable numbers of corpora lutea, necropsy, implantations, resorptions, and live fetuses among the groups. There were no treatment-related effects on reproductive or developmental parameters at dose levels up to and including the limit dose [1000 mq/kq/day]. The maternal NOEL in this range-finding study is 1000 mg/kg/day [limit dose], the highest dose tested. The developmental NOEL is 1000 mg/kg/day, the limit dose.

This non-guideline [§83-3(b)] prenatal developmental toxicity range-finding study in the rabbit is classified <u>Acceptable</u>.

[6] MRID 44080321 - In a 2-generation reproduction study, Fluroxypyr [99.0% a.i.] was administered to 30 Sprague-Dawley rats/sex/dose via the diet at dose levels of 0, 100, 500, and 750 mg/kg/day [males] and 0, 100, 500, and 1000 mg/kg/day [females] during the pre-mating period of 10 weeks [F1 generation]/12 weeks [F2 generation]: There was one litter [F1] in the first generation and two litters [F2A and F2B] in , the second generation. Treatment-related deaths due to renal failure occurred in both sexes at the high dose in both generations {1 P1 male [day 100], 2 P1 females [days 48 & 71], 1 P2 male [day 112], 1 P2 female [day 50] }. Males of both generations displayed lower body weights [P1 (91-94% of control); P2 (89-93% of control)] and body-weight gains [P1 (93%)/P2 (91% of control)] during the dosing period and overall. Body weight and body-weight gain were comparable among the P1 females throughout the dosing period, but the P2 females displayed lower body weight [88-94% of control] and body weight gain [91% of control] during the dosing period. Food consumption was comparable among the P1 rats of both sexes during the dosing period, but decreased food consumption was noted in the P2 rats of both sexes. The effects observed increased progressively with time of exposure. During gestation, body weights were comparable among the P1 dams, and progressively lower than the controls at the high-dose level for the P2 dams during both gestation periods [1" 88-92% of control/2™ 86-91% of control]. Bodyweight gains were progressively lower than the controls with each subsequent gestation period [P1 86%/1" P2 82%/2™ P2 74% of control]. During lactation, all dams of both generations displayed body weights that were initially lower than control values but by day 21 of lactation were comparable to the control values. Body-weight gains during lactation were greater than the controls at the mid- and high-dose levels [dose-related] for both generations and both litters of the P2 generation, and this effect increased progressively with time of exposure. There were increases in kidney weight with corresponding gross and microscopic findings [papillary atrophy; edema, necrosis, hyperplasia of the pelvic epithelium, degeneration/regeneration of the tubular tubulo-interstitial nephritis, and dilatation of the tubules] at the high-dose level in both sexes [both generations] and to a lesser degree in the mid-dose males [second generation]. Decreased absolute liver

weight was observed in the high-dose males of both generations and in the high-dose females in the second generation, which was attributed to the nutritional status, lower body weights, and decreased abdominal fat of these rats. Reproductive indices (mating performance, fertility, gestation length, time to mating, and the pup sex ratio) of both generations were not adversely affected by exposure to Fluroxypyr up to the limit dose in females and 750 mg/kg/day in males. Pup survival [F2A vs 98.9%/F2B 92.1% <u>vs</u> 99.7% high dose <u>vs</u> control] consequently litter sizes were decreased slightly in the F2A and F2B litters at the high-dose level. The author attributed the decrease to a few dams with compromised heath, as evidenced by their decreased amount of body fat and moderate to severe renal disease, although this was not very apparent from the data as presented. There were no apparent effects observed on pups at the mid- or low-dose level. F1 pup body weight at the high-dose level was comparable to the control during lactation, but body-weight gain was initially [day 1-4] lower than the control [do 81%.00 88% of control]. Decreased body weight was observed throughout lactation in both the F2A [dd 85%-91%/99 86%-92% of control] and F2B pups [dd 86%-92%/99 89%-94% of control; P2 89-93% of control]. Decreased body-weight gain was observed throughout lactation for both the F2A and F2B pups, but the magnitude of the decrease was greatest initially [days 1-4]. Overall, body-weight gain during lactation was only slightly lower than the control for both the F2A [or 90%/99 92% of control] and F2B [or 92%/99 94% of control] pups. The NOEL for maternal/paternal toxicity is 500/100 mg/kg/day], and the LOEL is 1000/500 mg/kg/day], based on death in females and increased kidney weight with corresponding gross and microscopic findings [papillary edema, necrosis, hyperplasia of the pelvic epithelium, degeneration/regeneration of tubular epithelium, the interstitial nephritis, and dilatation of the tubules] in both sexes. The reproductive NOEL is 1000/750 mg/kg/day], the highest dose tested. The neonatal NOEL is 500 mg/kg/day, and the LOEL is 1000 mg/kg/day, based on decreased pup body weight/body-weight gain and slightly lower survival.

This guideline [§83-4; OPPTS 870.3800] 2-generation reproduction study in rats is classified <u>Acceptable</u>.

[7] MRID 44080322 - In the combined chronic toxicity/carcinogenicity study in rats, Fluroxypyr [99.0% a.i.] was administered to 50 Fischer 344 rats/sex/dose via the diet at dose levels of 0, 100, 500, and 1000 [females only] mg/kg/day for 24 months [10 rats/sex/dose for 12 months]. At the high-dose level, there was an increase in death of both sexes, and the males at this dose level were terminated on day 118 [6 deaths prior to day I12] following erratic body-weight gains, changes in clinical chemistry findings indicative of impaired renal function, and a thin appearance. The high-dose females had a 42% mortality rate, with 48% of the deaths attributed to renal failure. Body-weight gain during the first 90-day interval was decreased [79% of control] in males at the high dose but comparable to control for females. Overall body-weight gain of the high-dose females was decreased [69% of control] compared to the control. Food consumption was not adversely affected overall. There were no consistent findings in hematology, clinical chemistry, or urinalysis parameters monitored, although the changes noted on several occasions were consistent with kidney effects

. and/or nutritional condition of the rat. Kidney weight was increased at the 500 mg/kg/day dose level in males and at all three dose levels in females, although the increase at the low-dose level appears to be within that of the historical control. Gross and microscopic lesions characteristic of renal toxicity [decreased size, papillary necrosis, and roughened surface] were observed in the high-dose males sacrificed study termination, chronic progressive 118. Αt glomerulonephropathy [CPG] of a severe or very severe degree was slightly increased in males at 500 mg/kg/day when compared to the lowdose and control males and was slightly higher than the historical control. In females at study termination, increased severity of renal CPG was observed at the 500 and 1000 mg/kg/day dose levels, compared to the control and low-dose groups. Other changes observed [decreased body qastric erosion/ulcers of glandular mucosal were considered the nutritional state of secondary changes due to Histologically, hyperplasia of the pelvic epithelium, papillary necrosis, and tubular nephrosis were observed at the 500 mg/kg/day in males and at 1000 mg/kg/day in females at study termination. There was no apparent increase in the incidence of kidney tumors in either sex. With the exception of an increased incidence of parafollicular cell adenomas [single only] in males at 500 mg/kg/day, at the doses tested, there was no apparent treatment-related increase in any tumor type in either sex. The LOEL is 500 mg/kg/day], based on increased kidney weight in both sexes, increased incidence of atrophy, adipose tissue [mesenteric tissues] in males and an increase in the severity of chronic progressive glomerulonephropathy in the kidney in both sexes. The NOEL is 100 mg/kg/day]. Deaths occurred at 1000 mg/kg/day in males within the first 90 days on test [2 by day 28 and 3 more by day 56].

This guideline [§83-5] combined chronic toxicity/ carcinogenicity study in the rat is Acceptable.

[8] MRID 44094901 - Under the conditions of this developmental toxicity study, the administration of Fluroxypyr methylheptyl ester [95.8% a.i.] to 28 naturally-mated female Sprague-Dawley CD<sup>®</sup> [SD] BR rats/group via gavage at dose levels of 0 [Mazola $^{\odot}$  corn oil], 100, 300, and 600. mg/kg/day from days 6 through 15 of gestation resulted 8 deaths [following 4, 6, 7, 7, 8, 8, 10, 10 days of dosing] at the high-dose level and decreased body-weight gain [77% of control] and food consumption during the dosing period at this dose level also. Clinical signs observed in those dying on test included staining of the skin/fur in the ano-genital area, lethargy, hypothermia, labored breathing, irregular gait, pale appearance]. Excessive salivation was observed only in the treated dams, and although the incidence increased with dose, it is not clear whether this is a direct systemic effect of the test material or due to residual amounts of the test material in the buccal cavity from the dosing procedure. There were no treatmentrelated effects on gross pathologic alterations or absolute and relative liver - and kidney weights at any dose level. Comparable pregnancy rates were observed among the groups, and there were no abortions, premature deliveries, or dams with 100% intrauterine deaths [except one mid-dose dam]. All dams had live fetuses at necropsy, and there were comparable numbers of corpora lutea, implantations, resorptions, and live fetuses among the groups. There were no dead

fetuses. Fetal body weights and sex ratio were comparable among the there were no external malformations, malformations or variations, or skeletal malformations that could be attributed to treatment. The overall incidences of fetuses and litters with fetuses with one or more ossification variation was comparable among the groups, but there was an increase in the incidences of incompletely ossified cervical vertebral transverse processes [mid- and high-dose levels, not dose-related] and incompletely ossified pubes at the high-dose level compared to the concurrent and historical controls. These increases occurred at a dose level that resulted in severe maternal toxicity [death]. The maternal NOEL is 300 mg/kg/day, the LOEL is 600 mg/kg/day, based on deaths and decreased body-weight gain and food consumption. The developmental toxicity NOEL is 300 mg/kg/day, and the LOEL is 600 mg/kg/day, based on an increase in two ossification [incompletely ossified cervical vertebral transverse variations processes and pubes].

This guideline [§83-3(a)] prenatal developmental toxicity study in the rat is classified <a href="Acceptable">Acceptable</a>.

[9] MRID 44080323 - In independently performed microbial preincubation mutagenicity assays, Salmonella typhimurium strains TA1535, TA1537, TA98 and TA100 and Escherichia coli strain WP2uvrA were exposed to 100-5000  $\mu$ g/plate fluroxypyr methylheptyl ester (95.8%) in the presence and absence of S9 activation. The S9 fraction was derived from Aroclor 1254 induced rat livers and the test material was delivered to the test system in dimethyl sulfoxide. Slight compound precipitation was seen at  $\geq 2500 \ \mu$ g/plate +/-S9. Cytotoxicity was not apparent at any dose. All strains responded in the expected manner to the appropriate positive control. There was no indication that fluroxypyr methylheptyl ester induced a mutagenic effect at any dose with or without S9 activation.

This guideline [§84-2] bacterial gene mutation assay is classified. Acceptable.

[10] MRID 44080324 - In independently performed in vitro mammalian cell gene mutation assays, Chinese hamster ovary (CHO) cells were exposed to fluroxypyr methylheptyl ester (95.8%) doses of 1.25-50.0  $\mu$ g/mL without S9 activation (Trial 1) or 2:5-40  $\mu$ g/mL -S9 (Trial 2). In the presence of S9 activation, doses of 100-1178  $\mu$ g/mL or 100-1200  $\mu$ g/mL were processed in Trials 1 and 2, respectively. The S9 fraction was derived from Aroclor 1254 induced rat livers and the test material was delivered to the test system in dimethyl sulfoxide. No cells survived treatment with nonactivated doses ≥30 µq/mL and compound insolubility was seen at  $\ge 20~\mu \text{g/mL}$  -S9. With S9 activation, the test material was not cytotoxic at any dose; however, compound insolubility occurred at all assayed levels in both trials. The nonactivated and S9-activated positive controls induced the expected mutagenic response. There was no indication that fluroxypyr methylheptyl ester induced a mutagenic effect in the absence or presence of S9 activation. However, the failure to test at least one fully soluble dose under S9 activated conditions was not explained and precludes acceptance of the data from this phase of testing as valid.

This guideline [§84-2] mammalian cell gene mutation assay is currently classified <u>Unacceptable</u>, but the study may be upgraded if the sponsor adequately explains the rationale for not testing a soluble dose; otherwise, the S9-activated portion of this assay should be repeated with a concentration range that includes at least one fully soluble test material concentration.

[11] MRID 44080325 - In independently performed in vitro cytogenetic assays, lymphocytes harvested from two male Sprague Dawley rats per trial were exposed to fluroxypyr methylheptyl ester nonactivated doses of 0.42-1250  $\mu \text{g/mL}$  for 24 hours and comparable S9activated doses for 4 hours with a cell harvest at 20 hrs (Trial 1). For Trial 2, cells were treated with 12.5-270  $\mu q/mL +/-S9$  as described for Trial 1; additional cultures were exposed to a comparable dose range and harvested at 48 hours (24 hrs. posttreatment with the nonactivated test substance or 44 hrs. after a 4-hr. treatment with the S9-activated test material). The S9 fraction was derived from Aroclor 1254-induced rat livers and the test material was delivered to the test system in dimethyl sulfoxide. Cytotoxicity was observed at  $\geq 270~\mu \text{g/mL}$ +/-S9. The positive controls induced the expected high yield of cells with structural chromosome aberrations. There was no evidence that fluroxypyr methylheptyl ester induced a clastogenic response at any nonactivated or S9-activated dose.

This guideline [§84-2] <u>in vitro</u> mammalian cell cytogenetic assay is classified <u>Acceptable</u>.

[12] MRID 44080326 - In a mouse micronucleus assay, groups of five male and five female CD-1 (ICR) mice received single oral gavage administrations of 225, 450 or 900 mg/kg fluroxypyr methylheptyl ester (95.8%). The test material was delivered to the animals in corn oil. Animals were sacrificed at 24, 48 and 72 hours postadministration and harvested bone marrow cells were examined for the incidence of micronucleated polychromatic erythrocytes (MPEs). Toxic signs, similar to those seen in the preliminary range-finding studies (i.e., death, decreased activity and perineal soiling) were recorded for the high-dose group. No bone marrow cytotoxicity was seen at any dose or sacrifice time. The positive control induced the expected high yield of MPEs in males and females. There was no evidence that fluroxypyr methylheptyl ester induced a clastogenic or aneugenic effect in either sex at any dose or sacrifice time.

This guideline [§84-2] in vivo cytogenetic mutagenicity study is classified <u>Acceptable</u>.

[13] MRID 44080327 - In a metabolism study (MRID 44080327), Fluroxypyr <sup>14</sup>C- methylheptyl ester [95.8 % a.i. unlabeled; radiochemical purity 99%; labeled on the methylheptanol portion of the molecule] or <sup>14</sup>C-methylheptanol [98.9% unlabeled; radiochemical purity 97.5%) was administered to 5 [plasma]/3 [balance] male Fischer 344 rats/group in single oral [equimolar] doses of 50 mg Fluroxypyr methylheptyl ester/kg body weight or 17.7 mg Methylheptanol/kg body weight. The total recovery of the administered dose was 105% and 104%, with the principal

route of excretion being expired 14CO2, which contained ≈61% and 63% of the radioactivity for the fluroxypyr MHE and methylheptanol balance groups, respectively. The urine contained ~30% and 27% and the feces contained 5% and 7% of the administered dose for the Fluroxypyr MHE and Methylheptanol groups, respectively. At 48 hours post dose, ≈7% of the administered dose was recovered in the blood, carcass, and skin of both groups. The overall rates and routes of elimination were comparable between the groups. Each was extensively absorbed and eliminated. Approximately 52% and 54% of the administered Fluroxypyr MHE and Methylheptanol, respectively, was absorbed and expired as 14CO, within 12 hours post dose, and an additional 18% of the administered dose was excreted in the urine within 12 hours post dose. Based on the percentage of the dose in the expired <sup>14</sup>CO<sub>2</sub>, urine, and tissues, ≈90% of the dose was absorbed by the rats in each case. Once absorbed, both were extensively metabolized [20-22 metabolites] and rapidly expired as  $^{14}\mathrm{CO}_{\gamma}$  and eliminated in the urine with a half-life of 6 hours. Fluroxypyr MHE displayed a slower absorption rate than Methylheptanol, but once absorbed, the pharmacokinetic parameters were similar. Peak plasma concentrations of <sup>14</sup>C-radioactivity were attained by 7 and 10 hours post dose, and the half-lives for the elimination phase were ≈18.2 and 17.4 hours for Fluroxypyr MHE and Methylheptanol, respectively. It was stated that the percentage of radioactivity recovered in the tissues and carcass [≈7%] suggests 14C-incorporation into the carbon pool that may account for the longer half life in plasma as compared to the urinary half-life of 6 hours. Average area under the curve values were 140  $\mu$ g eg hr/g and 163  $\mu$ g eg hr/g for the Fluroxypyr MHE and Methylheptanol groups, respectively. Clearance values were comparable for these groups also [2.1 and 1.8 mL/min kg]. These pharmacokinetic parameters indicate no difference in kinetics of Methylheptanol, based on whether it is labeled alone or as part of the Fluroxypyr MHE molecule. Urine profiles were similar and indicated extensive metabolism [20-22 metabolites]. Unchanged Fluroxypyr MHE was not detected in any of the samples, and the author stated that this "is consistent with the majority of the dose metabolized to CO1." The data indicate that the Fluroxypyr MHE bond is readily hydrolyzed and that the methylheptyl ester portion of Fluroxypyr is bioequivalent to Methylheptanol.

This nonguideline metabolism study [§85-1] in the rat is classified <u>Acceptable</u>.

[14] MRID 44080329 - Under the conditions of the study, the acute oral LD<sub>50</sub> of XRM-5316 [25.6%] to Fischer 344 rats [dose levels of 500, 2000, and 5000 mg/kg; 5/sex/dose; 6-7 weeks old; fasted; 14-day observation period] was calculated to be 3738 mg/kg for male rats and 3162 mg/kg for female rats. Signs of toxicity included death [all high-dose females on day 1 and all but one high-dose male on days 1 and 2,] decreased—activity, incoordination, lacrimation, salivation, and labored breathing. This guideline [§81-1] acute oral toxicity study is classified Acceptable. TOXICITY CATEGORY: III

[15] MRID 44080330 - Under the conditions of the study, the acute dermal  $LD_{50}$  of XRM-5316 [25.6%] to New Zealand rabbits [5/sex/dose; 14-

1 /2

day observation period) was >2000 mg/kg for each sex. This guideline [§81-2] acute dermal toxicity study is classified Acceptable. TOXICITY CATEGORY: III

[16] MRID 44080331 - In an acute inhalation study, Fischer 344 rats [5 rats/sex] were exposed <u>via</u> inhalation [nose only] to the limit dose [5 mg/L] of XRM-5316 [25.6% a.i.] for a single 4-hour period. There were no adverse effects observed. The 4-hour  $LC_{50}$  was greater than 6.2 mg/L aerosolized XRM-5316 [Fluroxypyr methylheptyl ester]. XRM-5316 is TOXICITY CATEGORY IV for acute inhalation.

This guideline [§81-3] acute inhalation study in the rat is classified <u>Acceptable</u>.

[17] MRID 44080332 - In a primary eye irritation study, New Zealand White rabbits [2 males, 4 female] were exposed via the conjunctival sac of the right eye to a 0.1 mL aliquot of XRM-5316 [ 25.6% a.i.]. The left eye of each rabbit served as a control. The eyes were observed for eye irritation at 1, 24, 48, and 72 hours and 7, 14, and 21 days post dose. The study was terminated after 21 days post dose. Irritation was scored by the method of Draize, although not identified as such. Ocular irritation was observed in all rabbits at 1 hour post dose. Reddening of the iris was observed in only one [male] rabbit at 1 hour post dose only. Corneal opacity [grade 1] was observed in all rabbits at the 1-, 24-, 48-, and 72-hour time points, but only one rabbit [female] displayed this lesion at the day 7 time point. Slight to marked redness, chemosis, and ocular discharge were observed in all rabbits. By day 14, with the exception of 3 rabbits [females] who displayed slight conjunctival redness, all signs of ocular irritation had subsided. By day 21 post dose, all signs of ocular irritation had dissipated. In this study, Fluroxypyr methylheptyl ester is an eye irritant. Fluroxypyr methylheptyl ester is TOXICITY CATEGORY II for primary eye irritation based on the findings of corneal opacity [which resolved within 7 days in 5 rabbits and by day 14 in the remaining rabbit] and slight to marked redness, chemosis, and ocular discharge of the conjunctivae [resolved by day 21].

This guideline [§81-4] primary eye irritation study is classified Acceptable.

[18] MRID 44080333 - In a primary dermal irritation study, New Zealand White rabbits [5 males, 1 female] were dermally exposed to a 0.5 mL aliquot of XRM-5316 [25.6 % a.i.] for 4 hours to 6.25 cm² on their backs/fianks. The test sites were observed for dermal irritation within 15 and 30 minutes, 4 and 24 hours, 48 and 72 hours post dose. Irritation was scored by the method of Draize, although not identified as such. In this study, XRM-5316 was slight dermal irritant. All observations of erythema and edema were resolved by 48 hours. XRM-5316 is TOXICITY CATEGORY IV for primary dermal irritation.

This guideline [§81-5] primary dermal irritation study in the rabbit is classified <a href="Acceptable">Acceptable</a>.

1 : 2

[19] MRID 44080334 - In a dermal sensitization study with XRM-5316 [25.6%], Hartley guinea pigs [10 males] were tested using the Buehler Method. XRM-5316 was not a dermal sensitizer under the conditions of the study. This guideline [§81-6] dermal sensitization study in the guinea pig is classified as <a href="Acceptable">Acceptable</a>.

DISCREPANCIES: In the mouse carcinogenicity study, the metabolism study, and the 90-day rat study, the CAS No. for Fluroxypyr is listed as 69377-81-7. In the 2-generation reproduction study, the CAS No. is listed as 81406-37-3 for Fluroxypyr. The metabolism and mutagenicity studies list 81406-37-3 as the CAS No. for Fluroxypyr methylheptyl ester. The Material Safety Data Sheet for Fluroxypyr, 1-methylheptyl ester in MRID 44094901 [rat developmental toxicity study] lists a CAS No. of 81406-37-3. For the record, the Registrant should reconcile these differences. In MRID 44080324 [in vitro mammalian cell gene mutation assays], the study is currently classified as Unacceptable and does not satisfy the quideline requirements [§84-2] for mammalian cell gene mutation mutagenicity data. It may be upgraded if the Registrant adequately explains the rationale for not testing a soluble dose; otherwise, the S9-activated portion of this assay should be repeated with a concentration range that includes at least one fully soluble test material concentration.

Robert F. Bischoff DowElanco 9330 Zionsville Road Indianapolis, IN 46268

OCT | 1997

Dear Mr. Bischoff:

Subject:

Fluroxypyr Application for Pesticide Registration

Starane F (EPA File Symbol 62719-EIL) Starane EC (EPA File Symbol 62719-EIA)

EPA Petition No. 6F4772

Your Submission Dated August 6, 1996

The Agency has completed initial reviews of the application for pesticide registration referenced above. The following comments apply regarding the ecological effects data provided with this application:

- 1) Most of the ecological effects data submitted to support this application were found to be acceptable. The exceptions are described in comments #2, 3, and 4 below.
- The aquatic plant study testing the effects of fluroxypyr on *Navicula pelliculosa* (MRID #440803-39, §123-2) was found to be unacceptable as submitted. The study may be upgraded with the submission of the additional information as described in the enclosed review dated July 28, 1997.
- The estuarine/marine study testing the effects of fluroxypyr on the shell deposition of oysters (MRID #440803-10, §72-3b) was found to be unacceptable and cannot be repaired. Please refer to the enclosed review dated July 28, 1997.
- The aquatic invertebrate study testing the effects of fluroxypyr on *Daphnia magna* (MRID #440803-14, §72-4) was found to be unacceptable as submitted. The study may be upgraded with the submission of the additional information as described in the enclosed review dated July 30, 1997.

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DK:30	5-7546:1	4B/PM23	С	ONCURRENCES	 -		
SYMBOL .	7505C						
SURHAME .	D. KENNY				'		
DATE .	10/1/97						

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Complete copies of the reviews are included with this letter to provide the details of the reviews and the reasoning behind the above decisions. You will be notified upon the completion of the remaining reviews.

Sincerely yours,

Joanne I. Miller Product Manager (23) Herbicide Branch Registration Division (7505C)

Enclosure



# UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

#### **MEMORANDUM**

SUBJECT: Data Evaluation Records for Fluroxypyr 1-methylheptyl ester

(Chemical # 128968), ID # 062719-EIL STARANE F, Case # 060640,

Bar Code # D236845 sub-bean for D237735)

FROM:

Renee Costello Centre Contillo 7130/97

Environmental Risk Branch II

Environmental Fate and Effects Division 7507C

THRU:

Elizabeth M. Leovey, Chief

Environmental Risk Branch II

Environmental Fate and Effects Division 75076

TO:

Joanne Miller (23)

Registration Division (7505C)

EFED has completed review of seven ecological effects studies for fluroxypyr 1-methylheptyl ester (chemical # 128968). One of these studies was unacceptable for fulfilling guideline requirements. The chronic aquatic invertebrate study testing the effects of fluroxypyr 1-methylheptyl on *Daphnia magna* (Guideline 72-4, MRID 440803-14) is supplemental because the test was conducted at levels higher than the solubility limit and the actual test concentrations to which the organisms were exposed is unknown. This study may be upgraded if the registrant submits data on undissolved test material and information about filtration or centrifugation of test material (if it exists) and these data are judged to be adequate. The other six studies were classified as core and fulfil the guideline requirements.

0.031 lb ai/A

MRID 440803-35: This study is scientifically sound and fulfills the guideline requirements for a vegetative vigor study with terrestrial plants. Results Synopsis: Most sensitive monocot: Onion; Most sensitive parameter: phytotoxicity;  $EC_{25}$ : 0.124 lb ai/A; NOEL: 0.062 lb ai/A; Most sensitive dicot: Cotton; Most sensitive parameter: phytotoxicity;  $EC_{25}$ : 0.0012 lb ai/A; NOEL: 0.0010 lb ai/A

MRID 440803-36: This study is scientifically sound and fulfills the guideline requirements for an algal toxicity test. The 120-hour  $EC_{50}$  and NOEC for *A. flos-aquae* exposed to fluroxypyr 1-methylheptyl ester were 395 and 30 ppb, respectively.

MRID 440803-37: This study is scientifically sound and fulfills the guideline requirements for an algal toxicity test. The 120-hour EC<sub>50</sub> and NOEC for *S. costatum* exposed to fluroxypyr 1-methylheptyl ester were 292 and 179 ppb, respectively.

MRID 440803-38: This study is scientifically sound and fulfills the guideline requirements for an aquatic plant toxicity test. The EC<sub>50</sub> is > 2310 ppb and the NOEC is 1220 ppb.

MRID 440803-40: This study is scientifically sound and fulfills the guideline requirements for an algal toxicity test. The 96-hour  $EC_{50}$  and NOEC for *S. capricornutum* exposed to fluroxypyr 1-methylheptyl ester were > 1410 and 199 ppb, respectively.

Please forward copies of the DERs to the registrant as soon as possible. The information requested for MRID 440803-14 is needed to complete the Section 3 ecological risk assessment.

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#### Summary of Data Reviews

Guideline	Study Type	Test Species	MRID	Acceptability
	Fluro	cypyr 1-methylheptyl e	ester	
72-4	Invertebrate life- cycle	Daphnia magna	440803-14	Supplemental
123-1	Terrestrial plant vegetative vigor	10 terrestrial plant species	440803-35	Core .
123-1	Terrestrial plant seedling emergence	10 terrestrial plant species	440803-35	Core
123-2	Aquatic plant LC <sub>50</sub>	Blue-green alga ( <i>Anabaena flos-</i> <i>aquae)</i>	440803-36	Core
123-2	Aquatic plant LC <sub>50</sub>	Skeletonema costatum	440803-37	Core
123-2	Aquatic plant LC <sub>50</sub>	Duckweed (Lemna gibba)	440803-38	Core
123-2	Aquatic plant LC <sub>50</sub>	Freshwater green alga (Selenastrum capricornutum)	440803-40	Core

#### **DER Conclusions**

MRID 440803-14: This study is scientifically sound but does not fulfill the guideline requirements for a freshwater invertebrate life-cycle test using *Daphnia magna*. Testing was conducted at above the solubility limit. It is likely that there was some undissolved test material in the system, this was not reported. Also, by placing the samples in acetonitrile, any suspended particles would have dissolved and the actual test concentrations to which the organisms were exposed is unknown. It is likely that the reported measured concentrations are an overestimate. This study is classified as Supplemental.

MRID 440803-35: This study is scientifically sound and fulfills the guideline requirements for a seedling emergence study with terrestrial plants. Results Synopsis: Most sensitive monocot: Ryegrass; Most sensitive parameter: phytotoxicity;  $EC_{25}$ : >0.25 lb ai/A; NOEL: 0.124 lb ai/A; Most sensitive dicot: Cucumber; Most sensitive parameter: phytotoxicity;  $EC_{25}$ : 0.075 lb ai/A; NOEL:

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### DATA EVALUATION RECORD ALGAE OR DIATOM EC 50 TEST GUIDELINE 123-2 (TIER II)

PC Code No.: 128959 CHEMICAL: Fluroxypyr

TEST MATERIAL: Fluroxypyr 1-methylheptyl ester Purity: 95.8%

CITATION:

D.P. Milazzo, J.M. Hugo, and M.D. Martin <u>Authors:</u>

Title: Fluroxypyr 1-Methylheptyl Ester: The

Toxicity to the Freshwater Green Alga,

Selenastrum capricornutum Printz

Study Completion Date: June 4, 1996

> Laboratory: Environmental Toxicology & Chemistry

> > Research Laboratory, The Dow Chemical

Company, Midland, MI

DowElanco, Indianapolis, IN

<u>Sponsor:</u>
<u>Laboratory Report ID</u>: ES-3076

DP Barcode: D231718 + D236845 (sub-bum)

MRID No.: 440803-40

Mark A. Mossler, M.S., Toxicologist, REVIEWED BY:

KBN Engineering and Applied Sciences, Inc.

Signature: Ment Mouser Date: 6/17/97

APPROVED BY: Pim Kosalwat, Ph.D., Senior Scientist,

KBN Engineering and Applied Sciences, Inc.

Bignature: P. KoSalwat

Date: 6/17/97

5.

APPROVED BY:

Signature: C. Revée Costillo

Date: 7/1/97

6. STUDY PARAMETERS:

> Definitive Test Duration: 96 hours

Type of Concentrations: Initial measured

CONCLUSIONS: This study is scientifically sound and fulfills the guideline requirements for an algal toxicity test. 96-hour EC<sub>50</sub> and NOEC for S. capricornutum exposed to fluroxypyr 1-methylheptyl ester were >1410 and 199 ppb, respectively.

#### 8. ADEQUACY OF THE STUDY:

A. Classification: Core

B. Rationale: N/A

C. Repairability: N/A

9. <u>GUIDELINE DEVIATIONS</u>: The concentration of solvent in the solvent control and treatment solutions was not specified. Additionally, the test was conducted for 96 hours, rather than 120 hours, as recommended.

## 10. SUBMISSION PURPOSE:

#### 11. MATERIALS AND METHODS:

#### A. Test Organisms

Guideline Criteria	Reported Information
Species Skeletonema costatum Anabaena flos-aquae Selenastrum capricornutum Navicula pelliculosa	Selenastrum capricornutum
Initial Number of Cells 3,000 - 10,000 cells/mL	10,000 cells/mL
Nutrients Standard formula, e.g. 20XAAP	Algal assay medium

#### B. Test System

Guideline Criteria	Reported Information
<u> 8olvent</u>	Acetone
<u>Temperature</u> Skeletonema: 20°C Others: 24-25°C	24.1-25.6°C
Light Intensity Anabaena: 2.0 KLux (±15%) Others: 4.0-5.0 KLux (±15%)	3.4-5.1 KLux

Guideline Criteria	Reported Information
<pre>Photoperiod    Skeletonema:     14 h light, 10 h dark or     16 h light, 8 h dark    Others: Continuous</pre>	Continuous
<b>pH</b> Skeletonema: approx. 8.0 Others: approx. 7.5	Initial: 7.1-7.2 Final: 7.5-7.7

# C. Test Design

Guideline Criteria	Reported Information
Dose range 2X or 3X progression	63, 126, 253, 506, 1010, and 2020 ppb
<u>Doses</u> at least 5	6
<pre>Controls negative and/or solvent</pre>	Negative and solvent (acetone) controls
Replicates per dose 3 or more	3
<u>Duration of test</u> 120 hours	96 hours
Daily observations were made?	Counts on days 2, 3, and 4
Method of Observations	Cellular counts
Maximum Labeled Rate	0.25 lb acid equivalents/acre

# 12. REPORTED RESULTS:

Guideline Criteria	Reported Information
Initial and <del>120</del> h cell densities were measured?	Yes
Control cell count at 120 hr 2X initial count?	Yes
Initial chemical concentrations measured? (Optional)	Yes

Guideline Criteria	Reported Information
Raw data included?	Yes

#### Dose Response "

Initial measured concentration (µg/L)	Avg. Cell Density (x 10° cells/mL)	% Inhibition*
Control	71.9	-
Solvent Control	98.0	. <b>-</b>
50	97.9	4
101	113.1	-11
199	93.8	8
390	85.7	16
754	67.2	34
1410	77.1	24

<sup>\*</sup>Inhibition was based upon comparison to the pooled control.

Other Significant Results: None reported.

#### Statistical Results for Cell Density:

Statistical Method: Visual interpretation and analysis of variance coupled with Dunnett's test

EC<sub>50</sub>: >1410 ppb 95% C.I.: N/A Probit Slope: N/A NOEC: 199 ppb

#### 13. <u>VERIFICATION OF STATISTICAL RESULTS</u>:

Statistical Method: Visual interpretation and Williams' test with comparison to the solvent control

EC<sub>50</sub>: >1410 ppb 95% C.I.: N/A ppb Probit Slope: N/A NOEC: 390 ppb

14. REVIEWER'S COMMENTS: The test material has a hydrolytic half-life of approximately three days. Therefore, about 75% of the material may have hydrolyzed to the acid form of fluroxypyr over the course of the test. When the ester and acid forms were quantified and summed at test termination,

recoveries ranged from 28 to 101% of nominal. The time-0 recoveries ranged from 71 to 81% of nominal. Although the form of the test material changed over the testing period, the reviewer believes that the initial measured concentrations serve as reliable values with which to estimate the  $EC_{50}$  value, since the material will behave similarly under natural conditions.

This study is scientifically sound and fulfills the guideline requirements for an algal toxicity test. The 96-hour  $EC_{50}$  and NOEC for S. capricornutum exposed to fluroxypyr 1-methylheptyl ester were >1410 and 199 ppb, respectively. This study can be categorized as Core.

Selenastrum cell density

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WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Sol. Con.	3	979562.000	979562.000	1029911.333
2	50 ppb	3	979233.000	979233.000	1029911.333
3	101 ppb	3	1130939.000	1130939.000	1029911.333
4	199 ppb	3	937818.333	937818.333	937818.333
5	390 ppb	3	856726.333	856726.333	856726.333
6	754 ppb	3	672234.000	672234.000	721551.000
7	1410 ppb	3	770868.000	770868.000	721551.000

Selenastrum cell density

File: sel Transform: NO TRANSFORMATION

WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2 O	F 2
IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Sol. Con.10	029911.333				
50 ppb1	029911.333	0.726		1.76	k = 1, v = 14
101 ppb10	029911.333	0.726		1.85	k = 2, v = 14
199 ppb 9	937818.333	0.602		1.88	k = 3, v = 14
390 ppb	856726.333	1.771		1.89	k = 4, v = 14
754 ppb '	721551.000	3.719	*	1.90	k = 5, v = 14
1410 ppb	721551.000	3.719	*	1.91	k = 6, v = 14

s = 84969.953

Note: df used for table values are approximate when v > 20.

## DATA EVALUATION RECORD AQUATIC PLANT ECso TEST GUIDELINE 123-2 (TIER II)

128933

PC Code No.: 128959 CHEMICAL: Fluroxypyr 1.

TEST MATERIAL: Fluroxypyr 1-methylheptyl ester Purity: 95.8% 2.

3. CITATION:

> H.D. Kirk, D.P. Milazzo, J.M. Hugo, and <u>Authors:</u>

> > M.D. Martin

Title: Fluroxypyr 1-Methylheptyl Ester: The

Toxicity to the Aquatic Plant, Duckweed

Lemna gibba L. G-3

Study Completion Date:

June 4, 1996

Environmental Toxicology & Chemistry Laboratory:

Research Laboratory, The Dow Chemical

Company, Midland, MI

Sponsor: DowElanco, Indianapolis, IN

Laboratory Report ID: DECO-ES-3074

DP Barcode: D231718 + 0 = 366445 (4 six - bean)

MRID No.: 440803-38

REVIEWED BY: Mark A. Mossler, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.

Signature: Tint Musels

Date: 6/17/87

Pim Kosalwat, Ph.D., Senior Scientist, APPROVED BY:

KBN Engineering and Applied Sciences, Inc.

P. Kosalwat Signature:

Date: 6/17/97

APPROVED BY:
Signature: C. Renée Costello

Date: 711197

STUDY PARAMETERS: 6.

> Definitive Test Duration: 14 days

Type of Concentrations: Initial measured

**CONCLUSIONS:** This study is scientifically sound and fulfills the guideline requirements for an aquatic plant toxicity test.

Results Synopsis:

 $EC_{50}$ : >2310 ppb

95% C.I.: N/A

NOEC: 1220 ppb Probit Slope: N/A

## 8. ADEQUACY OF THE STUDY:

A. Classification: Core.

B. Rationale: N/A.

C. Repairability: N/A.

9. <u>GUIDELINE DEVIATIONS</u>: The pH of the medium used for testing (≈8.2) was greater than recommended (5.0).

## 10. SUBMISSION PURPOSE:

#### 11. MATERIALS AND METHODS:

# A. Test Organisms

Guideline Criteria	Reported Information		
<u>Species</u> Lemna gibba	Lemna gibba		
Number of Plants/Fronds 5 plants, 3 fronds each	<pre>16 fronds/replicate (4 plants with 4 fronds each)</pre>		
Nutrients Standard formula, e.g. 20XAAP	20XAAM		

## B. Test System

Guideline Criteria	Reported Information
<u>Solvent</u>	Acetone
Temperature 25°C	25.0-25.2°C
Light Intensity 5.0 KLux (±15%)	4.3-6.4 KLux
<u>Photoperiod</u> Continuous	Continuous
<u>Test Bystem</u> Static or Renewal	Static
<u>рн</u> Approx. 5.0	8.3-9.1

# C. Test Design

Guideline Criteria	Reported Information
Dose range 2X or 3X progression	2X
<u>Doses</u> at least 5	188, 375, 750, 1500, and 3000 ppb
<pre>Controls negative and/or solvent</pre>	Negative and solvent controls
Replicates per dose 3 or more	3
<u>Duration of test</u> 14 days	14 days
Daily observations were made?	Counts on all three replicates only conducted on day 14 of the test
Method of Observations	Number of fronds
Maximum Labeled Rate	0.25 lb acid equivalents/A

# 12. REPORTED RESULTS:

Guideline Criteria	Reported Information
Initial and 14 day frond numbers were measured?	Yes
Control frond at 14 days $\geq 2X$ initial count?	Yes
Initial chemical concentrations measured? (Optional)	Yes
Raw data included?	Yes

19%

Dose Response

Initial measured concentration (#g/L)	Avg. Frond Number	% Inhibition*	14-day pH
Control	445	-	8.8-9.0
Solvent Control	. 434	-	9.0-9.1
176	371	16	8.8-9.0
289	420	5	9.0-9.1
744	437	1	9.1
1220	365	17	8.9-9.1
2310	. 319	28	8.8-9.0

<sup>\*</sup>Based on comparison to the pooled control.

Other Significant Results: None noted.

#### Statistical Results for Frond Number

Statistical Method: Visual interpretation and Dunnett's test

EC<sub>50</sub>: >2310 ppb 95% C.I.: N/A Probit Slope: N/A NOEC: 1220 ppb

#### 13. VERIFICATION OF STATISTICAL RESULTS:

Statistical Method: Visual interpretation and Williams' test with comparison to the solvent control

EC<sub>50</sub>: >2310 ppb 95% C.I.: N/A Probit Slope: N/A NOEC: 1220 ppb

14. REVIEWER'S COMMENTS: The test material has a hydrolytic half-life of approximately three days. Therefore, all of the material may have hydrolyzed to the acid form of fluroxypyr over the course of the test. When the ester and acid forms were quantified and summed at test termination, recoveries ranged from 76 to 99% of time-0 values. The time-0 recoveries ranged from 77 to 100% of nominal. Although the form of the test material changed over the testing period, the reviewer believes that the initial measured concentrations serve as reliable values with which to

estimate the  $EC_{50}$  value, since the material will behave similarly under natural conditions.

This study is scientifically sound and fulfills the guideline requirements for an aquatic plant toxicity test. The 14-day EC $_{50}$  and NOEC for L. gibba exposed to fluroxypyr 1-methylheptyl ester were >2310 and 1220 ppb, respectively. This study can be categorized as **Core**.

Lemna frond number

File: lem Transform: NO TRANSFORMATION

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N 	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Sol. Con.	3	434.333	434.333	434.333
2	176 ppb	3	370.667	370.667	409.222
3	· 289 ppb	3	420.333	420.333	409.222
4	744 ppb	3	436.667	436.667	409.222
5	1220 ppb	3	365.000	365.000	365.000
6	2310 ppb	3	318.667	318.667	318.667

Lemna frond number

File: lem Transform: NO TRANSFORMATION

WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2 O	F 2
IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Sol. Con. 176 ppb 289 ppb 744 ppb 1220 ppb 2310 ppb	434.333 409.222 409.222 409.222 365.000 318.667	0.585 0.585 0.585 1.615 2.695	*	1.78 1.87 1.90 1.92 1.93	k= 1, v=12 k= 2, v=12 k= 3, v=12 k= 4, v=12 k= 5, v=12

s = 52.573

Note: df used for table values are approximate when v > 20.

#### DATA EVALUATION RECORD ALGAE OR DIATOM EC<sub>50</sub> TEST GUIDELINE 123-2 (TIER II)

1. CHEMICAL: Fluroxypyr PC Code No.: 128959

2. TEST MATERIAL: Fluroxypyr 1-methylheptyl ester Purity: 95.8%

3. CITATION:

Authors: J.S. Hughes, M.M. Alexander, and L.A.

Conder

Title: Fluroxypyr 1-Methylheptyl Ester: The

Toxicity to Skeletonema costatum

Study Completion Date: May 31, 1996

Laboratory: Carolina Ecotox, Inc., Durham, NC

Sponsor: The Dow Chemical Company, Midland, MI

<u>Laboratory Report ID</u>: 10-04-1

DP Barcode: D231718 + 0 236 845 (50 h ham)

MRID No.: 440803-37

4. REVIEWED BY: Mark A. Mossler, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.

Signature: Collet Mines

APPROVED BY: Pim Kosalwat, Ph.D., Senior Scientist,

KBN Engineering and Applied Sciences, Inc.

signature: P. Hosalwat Date: 6/17/97

5. APPROVED BY:

Bignature: C Renée Costolo Date: 7/197

6. STUDY PARAMETERS:

Definitive Test Duration: 120 hours

Type of Concentrations: Initial measured

7. <u>CONCLUSIONS</u>: This study is scientifically sound and fulfills the guideline requirements for an algal toxicity test. The 120-hour EC<sub>50</sub> and NOEC for *S. costatum* exposed to fluroxypyr 1-methylheptyl ester were 292 and 179 ppb, respectively.

8. ADEQUACY OF THE STUDY:

A. Classification: Core

B. Rationale: N/A

200

- C. Repairability: N/A
- 9. **GUIDELINE DEVIATIONS:** No major guideline deviations were noted.

# 10. SUBMISSION PURPOSE:

# 11. MATERIALS AND METHODS:

# A. Test Organisms

Guideline Criteria	Reported Information
Species Skeletonema costatum Anabaena flos-aquae Selenastrum capricornutum Navicula pelliculosa	Skeletonema costatum
Initial Number of Cells 3,000 - 10,000 cells/mL	10,000 cells/mL
<u>Nutrients</u> Standard formula, e.g. 20XAAP	Marine algal assay medium with a salinity of 30%

# B. Test System

Guideline Criteria	Reported Information
<u>Solvent</u>	DMF
Temperature Skeletonema: 20°C Others: 24-25°C	21.2-21.7°C
Light Intensity Anabaena: 2.0 KLux (±15%) Others: 4.0-5.0 KLux (±15%)	3.8-4.7 KLux
Photoperiod  Skeletonema:  14 h light, 10 h dark or  16 h light, 8 h dark  Others: Continuous	14 h light, 10 h darκ
<u>pH</u> Skeletonema: approx. 8.0 Others: approx. 7.5	Initial: 8.2-8.3 Final: 8.2-8.8

# C. Test Design

Guideline Criteria	Reported Information
Dose range 2X or 3X progression	63, 126, 252, 503, 1005, and 2010 ppb, corrected for purity
<u>Doses</u> at least 5	6
<pre>Controls negative and/or solvent</pre>	Negative and solvent (0.5 mL/L DMF) controls
Replicates per dose 3 or more	3
<u>Duration of test</u> 120 hours	120 hours
Daily observations were made?	Counts on days 3, 4, and 5
Method of Observations	Cellular counts
Maximum Labeled Rate	0.25 lb acid equivalents/acre

# 12. REPORTED RESULTS:

Guideline Criteria	Reported Information
Initial and 120 h cell densities were measured?	Yes
Control cell count at 120 hr >2% initial count?	Yes
Initial chemical concentrations measured? (Optional)	Yes
Raw data included?	Yes

#### Dose Response

Initial measured concentration (µg/L)	$(x 10^4 \text{ cells/mL})$	% Inhibition*
Control	39.2	-
Solvent Control	38.9	-
43	39.4	-1
85	36.8	6
. 179	25.3**	3
347	7.5	81
798	0.3	99
1722	0.3	99

<sup>\*</sup>Inhibition was based upon comparison to the pooled control.

\*\*Replicate B of this group contained only 1% of the mean number of cells/mL in the other two replicates and was therefore omitted from analysis.

Other Significant Results: None noted.

#### Statistical Results for Cell Density:

Statistical Method: Non-linear regression analysis and analysis of variance coupled with Bonferroni's test

EC<sub>50</sub>: 246 ppb 95% C.I.: 166-365 ppb

Probit Slope: N/A NOEC: 179 ppb

#### 13. VERIFICATION OF STATISTICAL RESULTS:

Statistical Method: Moving average method and Bonferroni's test with comparison to the solvent control

EC<sub>50</sub>: 292 ppb 95% C.I.: 270-314 ppb

Probit Slope: N/A NOEC: 179 ppb

14. REVIEWER'S COMMENTS: The test material hydrolyzed to the acid form of fluroxypyr over the course of the test. When the ester and acid forms were quantified and summed at test termination (reviewer's calculations), recoveries ranged from 69 to 83% of nominal. The time-0 recoveries ranged from 68 to 86% of nominal. Although the form of the test material changed over the testing period, the reviewer believes that

the initial measured concentrations serve as reliable values with which to estimate the  $EC_{50}$  value, since the material will behave similarly under natural conditions.

Since the dose-response was not conducive to remodeling by non-linear regression analysis, the moving average method results were accepted as the reportable values. This study is scientifically sound and fulfills the guideline requirements for an algal toxicity test. The 120-hour EC<sub>50</sub> and NOEC for S. costatum exposed to fluroxypyr 1-methylheptyl ester were 292 and 179 ppb, respectively. This study can be categorized as **Core**.

Mossler fluroxypyr MHE Skeletonema costatum 5-29-97

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
798	100	99	99	0
347	100	81	81	0
179	100	3	3	0

BECAUSE THE NUMBER OF ORGANISMS USED WAS SO LARGE, THE 95 PERCENT CONFIDENCE INTERVALS CALCULATED FROM THE BINOMIAL PROBABILITY ARE UNRELIABLE. USE THE INTERVALS CALCULATED BY THE OTHER TESTS.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 274.2015

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN G LC50 95 PERCENT CONFIDENCE LIMITS 2 1.197027E-02 292.0532 270.2137 314.017

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS G H GOODNESS OF FIT PROBABILITY

14 128.6661 71.56998 0

A PROBABILITY OF O MEANS THAT IT IS LESS THAN 0.001.

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 8.095326

95 PERCENT CONFIDENCE LIMITS =-83.73084 AND 99.92149

LC50 = 284.0139

95 PERCENT CONFIDENCE LIMITS = 0 AND +INFINITY

LC10 = 197.906

95 PERCENT CONFIDENCE LIMITS = 0 AND +INFINITY

\*

Skeletonema cell density

File: skl Transform: SQUARE ROOT(Y)

	BONFERRONI t-TEST -	TABLE 1 OF 2	Ho:Contro	o1 <treatm< th=""><th>ent</th></treatm<>	ent
ROUP	IDENTIFICATION	TRANSFORMED MEAN	MEAN CALCULATED IN ORIGINAL UNITS	T STAT	SIG
1	Sol. Con.	622.783	388626.667		
2	43 ppb	627.951	394326.667	-0.161	
3	85 ppb	606.776	368400.000	0.498	
4	179 ppb	614.200	377360.000	0.239	
5	347 ppb	264.229	75433.333	11.157	*
6	798 ppb	.56.186	3166.667	17.630	*
7	1722 ppb	57.473	3316.667	17.590	* 

Sonferroni t table value = 2.75 (1 Tailed Value, P=0.05, df=13,6)

keletonema cell density

:: skl Transform: SQUARE ROOT(Y)

	BONFERRONI t-TEST -	TABLE	2 OF 2	Ho:Contr	ol <treatment< th=""></treatment<>
ROUP	IDENTIFICATION	NUM OF REPS	Minimum Sig Diff (IN ORIG. UNITS)	% of CONTROL	DIFFERENCE FROM CONTROL
1	Sol. Con.	3			
2	43 ppb	3	102129.838	26.3	-5700.000
3	85 ppb	3	102129.838	26.3	20226.667
4	179 ppb	2	113156.944	29.1	11266.667
5	347 ppb	3	102129.838	26.3	313193.333
6	798 ppb	3	102129.838	26.3	385460.000
7	1722 ppb	3	102129.838	26.3	385310.000

VOEC = 179/1

#### DATA EVALUATION RECORD ALGAE OR DIATOM EC<sub>50</sub> TEST GUIDELINE 123-2 (TIER II)

1. CHEMICAL: Fluroxypyr PC Code No.: 128959

2. TEST MATERIAL: Fluroxypyr 1-methylheptyl ester Purity: 95.8%

3. CITATION:

Authors: D.P. Milazzo, J.A. Miller, J.M. Hugo, and

M.D. Martin

Title: Fluroxypyr 1-Methylheptyl Ester: The

Toxicity to the Blue-Green Alga, Anabaena

flos-aquae

Study Completion Date: June 4, 1996

<u>Laboratory</u>: Environmental Toxicology & Chemistry

Research Laboratory, The Dow Chemical

Company, Midland, MI

Sponsor: DowElanco, Indianapolis, IN

Laboratory Report ID: ES-3073

DP Barcode: D231718 + 0 736845 (sub-barn)

MRID No.: 440803-36

4. REVIEWED BY: Mark A. Mossler, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.

Signature:

Man Finda

Date: 6/17/97

APPROVED BY: Max Feken, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.

Signature:

/ W/plen

Date: 6/17/97

5. APPROVED BY:

Bignature: C. Renée Costello

Date: 7/1197

s. <u>study parameters</u>:

Definitive Test Duration: 120 hours

Type of Concentrations: Initial measured

7. <u>CONCLUSIONS</u>: This study is scientifically sound and fulfills the guideline requirements for an algal toxicity test. The 120-hour EC<sub>50</sub> and NOEC for A. flos-aquae exposed to fluroxypyr 1-methylheptyl ester were 395 and 30 ppb, respectively.

## 8. ADEQUACY OF THE STUDY:

A. Classification: Core

B. Rationale: N/A

C. Repairability: N/A

9. <u>GUIDELINE DEVIATIONS</u>: The concentration of solvent in the solvent control and treatment solutions was not specified.

## 10. SUBMISSION PURPOSE:

#### 11. MATERIALS AND METHODS:

## A. Test Organisms

Guideline Criteria	Reported Information
<u>Species</u> Skeletonema costatum Anabaena flos-aquae Selenastrum capricornutum Navicula pelliculosa	Anabaena flos-aquae
Initial Number of Cells 3,000 - 10,000 cells/mL	10,000 cells/mL
<u>Nutrients</u> Standard formula, e.g. 20XAAP	Algal assay medium

## B. Test System

Guideline Criteria	Reported Information	
Solvent	Acetone	
Temperature Skeletonema: 20°C Others: 24-25°C	25.0-25.1°C	
Light Intensity Anabaena: 2.0 KLux (±15%) Others: 4.0-5.0 KLux (±15%)	1.8-2.3 KLux	

Guideline Criteria	Reported Information
Photoperiod Skeletonema: 14 h light, 10 h dark or 16 h light, 8 h dark Others: Continuous	Continuous
<u>pH</u> Skeletonema: approx. 8.0 Others: approx. 7.5	7.5-8.7

# C. Test Design

Guideline Criteria	Reported Information
Dose range 2X or 3X progression	30, 60, 120, 241, 481, and 961 ppb
<u>Doses</u> at least 5	6
<pre>Controls negative and/or solvent</pre>	Negative and solvent (acetone) controls
Replicates per dose 3 or more	3
<u>Duration of test</u> 120 hours	120 hours
Daily observations were made?	Counts on days 3, 4, and 5
Method of Observations	Cellular counts
Maximum Labeled Rate	0.25 lb acid equivalents/acre

# 12. REPORTED RESULTS:

Guideline Criteria	Reported Information
Initial and 120 h cell densities were measured?	Yes
Control cell count at 120 hr >2X initial count?	Yes
Initial chemical concentrations measured? (Optional)	Yes

Guideline Criteria	Reported Information
Raw data included?	Yes

#### Dose Response

Initial measured concentration (µg/L)	Avg. Cell Density (x 10 cells/mL)	% Inhibition*
Control	43.4	-
Solvent Control	44.1	-
· 30	58.1	-33
73	28.8	34
112	21.1	52
226	26.6	39
461	28.1	36
986	14.6	67

<sup>\*</sup>Inhibition was based upon comparison to the pooled control.

Other Significant Results: None reported.

#### Statistical Results for Cell Density:

Statistical Method: Least squares linear regression analysis and analysis of variance coupled with Dunnett's test

EC<sub>50</sub>: 395 ppb

95% C.I.: 21-7438 ppb

Probit Slope: N/A

NOEC: 73 ppb

#### 13. <u>VERIFICATION OF STATISTICAL RESULTS</u>:

Statistical Method: Moving average method and Williams' test with comparison to the solvent control

EC<sub>50</sub>: 602 ppb

95% C.I.: 434-999 ppb

Probit Slope: N/A

NOEC: 30 ppb

14. REVIEWER'S COMMENTS: The test material has a hydrolytic half-life of approximately three days. Therefore, about 75% of the material may have hydrolyzed to the acid form of fluroxypyr over the course of the test. When the ester and acid forms were quantified and summed at test termination,

900

recoveries ranged from 85 to 127% of nominal. The time 0 recoveries ranged from 90 to 116% of nominal. Although the form of the test material changed over the testing period, the reviewer believes that the initial measured concentrations serve as reliable values to estimate the EC $_{50}$  value on, since the material will behave similarly under natural conditions.

This study is scientifically sound and fulfills the guideline requirements for an algal toxicity test. The 120-hour EC<sub>50</sub> and NOEC for A. flos-aquae exposed to fluroxypyr 1-methylheptyl ester were 395 and 30 ppb, respectively. This study can be categorized as **Core**.

Anabaena cell density

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WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Sol. Con.	3	440736.000	440736.000	511074.167
2	30 ppb	3	581412.333	581412.333	511074.167
. 3	73 ppb	3	287977.333	287977.333	287977.333
4	112 ppb	3	210822.667	210822.667	252673.222
5	226 ppb	3	266065.667	266065.667	252673.222
6	461 ppb	3	281131.333	281131.333	252673.222
7	986 ppb	3	146109.333	146109.333	146109.333

Anabaena cell density

File: ana Transform: NO TRANSFORMATION

WILLIAMS TEST (Isotonic regression model) TABLE 2 OF 2 ISOTONIZED CALC. SIG TABLE DEGREES OF MEAN WILLIAMS P=.05 WILLIAMS IDENTIFICATION FREEDOM Sol. Con. 511074.167 30 ppb 511074.167
30 ppb 511074.167
73 ppb 287977.333
1.876
\*
112 ppb 252673.222
2.310
\*
226 ppb 252673.222
2.310
\*
461 ppb 252673.222
2.310
\*
986 ppb 146109.333
3.619 1.76 k = 1, v = 14k= 2, v=14 k= 3, v=14 1.85 1.88 k = 4, v = 14

1.90

k = 5, v = 14

1.91 k=6, v=14

= 99706.279

Note: df used for table values are approximate when v > 20.

NOTE: 30 ppt.

Mossler fluroxypyr MHE Anabaena flos-aquae 5-27-97

~~~~~		******	****	********
CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL
	EXPOSED	DEAD	DEAD	PROB. (PERCENT)
986	100 .	67	67	0
461	100	37	37	0
226	100	40	40	0
112	100	52	52	0
73	100	35	35	0

BECAUSE THE NUMBER OF ORGANISMS USED WAS SO LARGE, THE 95 PERCENT CONFIDENCE INTERVALS CALCULATED FROM THE BINOMIAL PROBABILITY ARE UNRELIABLE. USE THE INTERVALS CALCULATED BY THE OTHER TESTS.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 246.6023

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

 SPAN
 G
 LC50
 95 PERCENT CONFIDENCE LIMITS

 2
 .2595643
 602.3838
 434.3644
 999.3899

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS G H GOODNESS OF FIT PROBABILITY

2 6.708636 6.4106 0

A PROBABILITY OF 0 MEANS THAT IT IS LESS THAN 0.001.

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = .4314972

95 PERCENT CONFIDENCE LIMITS =-.6861252 AND 1.549119

LC50 = 405.4383

95 PERCENT CONFIDENCE LIMITS = 0 AND +INFINITY

LC10 = .4620447

95 PERCENT CONFIDENCE LIMITS = 0 AND 51.49171

## DATA EVALUATION RECORD SEEDLING EMERGENCE EC25 TEST § 123-1 (TIER II)

PC Code No.: 128959 1. CHEMICAL: Fluroxypyr

TEST MATERIAL: Fluroxypyr methylheptyl ester Purity: 26.9%

З. CITATION:

> D. Schwab Author:

Evaluating the Effects of Fluroxypyr-MHE Title:

on the Seedling Emergence and Vegetative Vigor of Non-Target Terrestrial Plants

Study Completion Date: May 7, 1996

> ABC Laboratories, Inc., Columbia, MO Laboratory:

DowElanco, Indianapolis, IN Sponsor:

<u>Laboratory Report ID:</u> 42838

MRID No.: 440803-35

DP Barcode: D231718 + D236845 (sub herea)

REVIEWED BY: Mark Mossler, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.

Signature: ( 12 - Million)

Pim Kosalwat, Ph.D., Senior Scientist

KBN Engineering and Applied Sciences, Inc. P. Kosalwat

Signature:

Date: 6/2/97

Date: . 4 42

APPROVED BY:

Bignature: C. Kensé Costello

Date: 7-11197

6. STUDY PARAMETERS:

APPROVED BY:

Definitive Study Duration: 21 or 28 days

7. **CONCLUSIONS:** This study is scientifically sound and fulfills the guideline requirements for a seedling emergence study with terrestrial plants.

Results Synopsis

Most sensitive monocot: Ryegrass

Most sensitive parameter: phytotoxicity

 $EC_{25}$ : >0.25 lb ai/A NOEL: 0.124 lb ai/A

Most sensitive dicot: Cucumber

Most sensitive parameter: phytotoxicity

EC<sub>25</sub>: 0.075 lb ai/A NOEL: 0.031 lb ai/A

#### 8. ADEQUACY OF THE STUDY:

A. Classification: Core.

B. Rationale: N/A.

C. Repairability: N/A.

9. <u>GUIDELINE DEVIATIONS</u>: The organic matter content of the soil (2.7%) was greater than recommended (1%).

#### 10. SUBMISSION PURPOSE:

#### 11. MATERIALS AND METHODS:

#### A. Test Organisms

Guideline Criteria	Reported Information	
Species 6 dicots in 4 families, including soybean and a rootcrop; 4 monocots in 2 families, including corn.	<pre>Dicots: cotton, cucumber, radish, soybean, sunflower, tomato Monocots: corn, onion, ryegrass, wheat</pre>	
Number of seeds per rep	10 (20 for tomato)	
Source of Seed	Commercial suppliers	
Historical % Germination of Seed	≥84%	

#### B. Test System

Guideline Criteria	Reported Information
Solvent	None
Site of test	Greenhouse
Planting method / type of pot	Planted within one day before application/10-cm square pots
Method of application	Track sprayer

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Guideline Criteria	Reported Information		
Method of watering	Overhead irrigation for 2 to 3 days, followed by subirrigation		
Growth stage at application Seed or plant.	Seed		

# C. Test Design

Guideline Criteria	Reported Information
Dose range 2x or 3x	2x: ranging from 0.55 g active ingredient (ai)/Ha to 280 g ai/Ha (0.0005 - 0.25 lb ai/A)
<b>Doses</b> At least 5	5, 6, 8, 9, or 10
Controls Negative and solvent	Negative (deionized water) and formulation blank controls
Replicates per dose At least 3	3 replicates
Duration of test 14 days	3 or 4 weeks
Were observations made at least weekly?	Only "final" rating reported
Maximum labeled rate	280 g ai/Ha (0.25 lb ai/A)

### 12. REPORTED RESULTS:

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes
Was an NOEL observed for each species?	Yes
Phytotoxic observations	Yes .
Were initial chemical concentrations measured? (Optional)	Yes, recoveries of selected spray solutions ranged between 97 and 108% of nominal

2/2

Guideline Criteria	Reported Information
Were adequate raw data included?	Yes

Results for the most sensitive parameter of each species\*

Species	Parameter	EC <sub>25</sub> (g ai/Ha)	NOEL (g ai/Ha)
Cotton	phytotoxicity	133	70
Cucumber	phytotoxicity	97	35
Radish	all parameters similar	>280	280
Soybean	phytotoxicity	266	70
Sunflower	phytotoxicity	118	70
Tomato	shoot fresh weight	164	140
Corn	all parameters similar	>280	280
Onion	all parameters similar	>280	280
Ryegrass	phytotoxicity	>280	140
Wheat	all parameters similar	>280	280

<sup>\*</sup>The most sensitive parameter is based on the EC25 value (except for ryegrass).

Observations: Symptoms of test material toxicity were mainly manifest as stunting, leaf rolling, and basal stem swelling.

Statistical Method: Dunnett's test was used for mean separation using pooled control data for all parameters except cucumber shoot length and tomato emergence. Comparisons for these two species were made against the formulation blank control. Nonlinear least squares regression was employed to determine the EC values.

13. <u>VERIFICATION OF STATISTICAL RESULTS</u>: All comparisons were made against the formulation blank control. Williams' test was used for mean separation. Probit analysis, visual interpretation, or linear interpolation was used for EC<sub>25</sub>

determination. Except for cucumber, the magnitude of effect (generally less than 50% at the highest rate) and a lack of appropriate dose-response precluded the use of non-linear regression analysis. Cucumber phytotoxicity was remodeled using non-linear regression. All concentrations were converted to 1b ai/A before analysis.

Results for the most sensitive parameter of each species

Species	Parameter	EC <sub>25</sub> (lb ai/A)	NOEL (lb ai/A)
Cotton	phytotoxicity	0.125	0.062
Cucumber	phytotoxicity	0.075	0.031
Radish	all parameters similar	>0.25	0.25
Soybean	phytotoxicity	0.24	0.062
Sunflower	phytotoxicity	0.109	0.062
Tomato	shoot fresh weight	0.142	0.124
Corn	all parameters similar	>0.25	0.25
Onion	all parameters similar	>0.25	0.25
Ryegrass	phytotoxicity	>0.25	0.124
Wheat	all parameters similar	>0.25	0.25

Results for most sensitive parameter of most sensitive species

	Monocot	Dicot
Species ryegrass		cucumber
Parameter	phytotoxicity	phytotoxicity
EC <sub>25</sub> (lb ai/A)	>0.25	0.075
95% C.I. (lb ai/A)	CNBD*	0.049 - 0.114
Probit Slope	N/A	1.9
NOEL (lb ai/A)	0.124	0.031

<sup>\*</sup>CNBD = Could not be determined.

14. REVIEWER'S COMMENTS: The terms of g ai/Ha. The review of converted the results in of lb ai/A. This study is scir converted the rates in terms the guideline requirements. The side is classified as Core.

Cotton phytotoxicity

File: cot Transform: ARC SINE(SQUARE ROOT()

WILLIAMS TEST (Isotonic regression TABLE 1 OF 2

GROUP	IDENTIFICATION	N	OPMEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1 2 3 4 5 6 7 8 9	Form. Con. 0.001 lb ai/A 0.002 lb ai/A 0.008 lb ai/A 0.015 lb ai/A 0.031 lb ai/A 0.062 lb ai/A 0.124 lb ai/A 0.25 lb ai/A	3 3 3 3 3 3 3 3 3 3	1.000 0.967 1.000 1.000 0.967 1.000 0.967 0.667	1.412 1.358 1.412 1.412 1.412 1.358 1.412 1.358 0.956 0.752	1.412 1.398 1.398 1.398 1.398 1.385 1.385 1.385 0.956 0.752

Cotton phytotoxicity

File: cot Transform: ARC SINE(SQUARE ROOT(Y))

	WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2 C	F 2
-	IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
_	Form. Con.	1.412				
	0.001 lb ai/A	1.398	0.287		1.72	k = 1, v = 20
	0.002 lb ai/A	1.398	0.287		1.81	k = 2, v = 20
	0.004 lb ai/A	1.398	0.287		1.83	k = 3, v = 20
	0.008 lb ai/A	1.398	0.287		1.85	k = 4, v = 20
	0.015 lb ai/A	1.385	0.574		1.86	k = 5, v = 20
	0.031 lb ai/A	1.385	0.574		1.86	k = 6, v = 20
	0.062 lb ai/A	1.358	1.148		1.86	k = 7, v = 20
	0.124 lb ai/A	0.956	9.632	*	1.87	k = 8, v = 20
	0.25 lb ai/A	0.752	13.949	*	1.87	k = 9. v = 20

s = 0.058

Note: df used for table values are approximate when v > 20.

NOTE - 6.062 16 a /A

# cotton phytotoxicity

## Estimated EC Values and Confidence Limits

		Lower	Upper
Point	Conc.	95% Confidence	
EC 1.00	0.0324		
EC 5.00	0.0565		
EC10.00	0.0759		
EC15.00	0.0926		
EC50.00	0.2154		
EC85.00	0.5006		
EC90.00	0.6112		
EC95.00	0.8215		
EC99.00	1.4305		

Y= 2.83(,)+6.89 EC25- 6.125 160 /A

Cucumber phytotoxicity

File: cuc Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	1.000	1.412	1.412
2	0.001 lb ai/A	3	1.000	1.412	1.412
3	0.002 lb ai/A	3	1.000	1.412	1.412
4	0.004 lb ai/A	3	1.000	1.412	1.412
5	0.008 lb ai/A	3	1.000	1.412	1.412
6	0.015 lb ai/A	3	1.000	1.412	1.412
7	0.031 lb ai/A	3	0.967	1.358	1.358
8	0.062 lb ai/A	3	0.800	1.116	1.116
9	0.124 lb ai/A	3	0.600	0.886	0.886
10	0.25 lb ai/A	3	0.467	0.752	0.752

Cucumber phytotoxicity

File: cuc Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS	TEST	(Isotonic	regression	model)	TABLE	2 0	F 2
	Τ.	COTONTOED	CATC	CIC	מזמגת		DE

IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Form. Con.	1.412				
0.001 lb ai/A	1.412	0.000		1.72	k = 1, v = 20
0.002 lb ai/A	1.412	0.000		1.81	k = 2, v = 20
0.004 lb ai/A	1.412	0.000		1.83	k = 3, v = 20
0.008 lb ai/A	1.412	0.000		1.85	k = 4, v = 20
0.015 lb ai/A	1.412	0.000		1.86	k = 5, v = 20
0.031 lb ai/A	1.358	1.238		1.86	k = 6, v = 20
0.062 lb ai/A	1.116	6.749	*	1.86	k = 7, v = 20
0.124 lb ai/A	0.886	11.982	*	1.87	k = 8, v = 20
0.25 lb ai/A	0.752	15.040	*	1.87	k = 9, v = 20

s = 0.054

Note: df used for table values are approximate when v > 20.

NOFL- 0.031 16 ac/A

## cucumber phytotoxicity

## Estimated EC Values and Confidence Limits

Point	Conc.	Lower 95% Confiden	Upper ce Limits
EC 1.00	0.0120	0.0059	0.0189
EC 5.00	0.0273	0.0170	0.0372
EC10.00	0.0423	0.0297	0.0538
EC15.00	0.0568	0.0429	0.0695
EC50.00	0.1981	0.1632	0.2577
EC85.00	0.6904	0.4704	1.2610
EC90.00	0.9277	0.5999	1.8496
EC95.00	1.4373	0.8584	3.2682
EC99.00	3.2666	1.6760	9.5355

y - 1.71.(x) + 6.34 EC2; + 6.689 16 a.71

```
WEIGHTED REGRESSION
                                                    13:26 Wednesday, May 21, 1997
               Non-Linear Least Squares Iterative Phase
Dependent Variable COUNT Method: Gauss-Newton
                 LOG EC25
      Iter
                                    SIGMA
                                                              Weighted SS
                 -1.051000
                                  0.523000
                                                  1.000000
                                                                 0.078225
                                 0.650376
                                                 1.028703
                                                                 0.066602
                -1.142072
                -1.124361
                                 0.629666
                                                 1.020146
                                                                 0.066379
                 -1.128678
                                 0.634756
                                                  1.021703
                                                                 0.066392
                                 0.633511
                 -1.127642
                                                  1.021317
                                                                 0.066387
                 -1.127896
                                 0.633815
                                                  1.021411
                                                                 0.066388
                 -1.127834
                                 0.633741
                                                  1.021388
                                                                 0.066387
                 -1.127849
                                 0.633759
                                                  1.021393
                                                                 0.066388
                -1.127845
                                  0.633755
                                                  1.021392
                                                                 0.066388
                -1.127846
                                  0.633756
                                                  1.021392
                                                                 0.066388
        10
                 -1.127846
                                  0.633755
                                                  1.021392
                                                                 0.066388
        11
                -1.127846
                                 0.633755
                                                  1.021392
                                                                 0.066388
NOTE: Convergence criterion met.
   Non-Linear Least Squares Summary Statistics
                                                     Dependent Variable COUNT
       Source
                                     Weighted SS
                                                      Weighted MS
       Regression
                                    11.500000000
                                                      3.83333333
       Residual
                                    0.066387556
                                                      0.005532296
       Uncorrected Total
                                    11.566387556
       (Corrected Total)
                                     0.992150134
       Parameter
                     Estimate
                                   Asymptotic
                                                           Asymptotic 95 %
                                   Std. Error
                                                       Confidence Interval
                                                       Lower
                                                                      Upper
       LOG EC25 -1.127845903 0.08436219301 -1.3116556020 -0.9440362036
          SIGMA
                  0.633755387 0.09293379924 0.4312697345 0.8362410392
                  1.021392303 0.04176156193 0.9304015417 1.1123830636
                        *Asymptotic Correlation Matrix
        Corr
                           LOG EC25
                                                  SIGMA
                                                                        C0
        LOG EC25
                                          -0.822348343
                                                              -0.826220663
                       -0.822348343
           $1GMA
                                                             0.5815601048
              CO
                       -0.826220663
                                          0.5815601048
    cucumber phytotoxicity

MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
                        SUMMARY OF NONLTHEAR REGRESSION
                                                    13:26 Wednesday, May 21, 1997
           CONC
    OBS
                   LOG EC25
                                  SIGMA
                                                        RESID SS
                                                                       EC25
                    -1.12785
                                0.63376
                                            1.02139
                                                        0.066388
                                                                     0.074500
                             cucumber phytotoxicity
    MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG CONC) / SIGMA - 0.67449)
                                                    T3:26 Wednesday, May 21, 1997
                 Plot of COUNT*LOG CONC. Symbol used is '0'.
                 Plot of PRED*LOG CONC. Symbol used is '.'.
COUNT
  1.1
```

||File:A:cuc.out | Page 2

```
|File:A:cuc.out Page 1
                              cucumber phytotoxicity
                                                    13:26 Wednesday, May 21, 1997
        OBS
                CONC
                        LOG CONC
                                      Y 1
                                             Y2
                                                     Y3
                                                           Y4
                                                                  Y5
                                                                        Y6
               0.000
               0.031
                        -1.50864
                                     0.9
                                            1.0
                                                    1.0
               0.062
                        -1.20761
                                     0.8
                                            0.7
                                                   0.9
               0.124
                        -0.90658
                                                   0.6
                                     0.6
                                            0.6
               0.250
                        -0.60206
                                     0.4
                                            0.5
                                                   0.5
                             cucumber phytotoxicity
         MODEL: COUNT = CO * PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
                              WEIGHTED REGRESSION
                                                    13:26 Wednesday, May 21, 1997
                    Non-Linear Least Squares Iterative Phase
                Dependent Variable COUNT Method: Gauss-Newton
      Iter
                  LOG EC50
                                     SIGMA
                                                              Weighted SS
                 -0.703000
                                                                  0.078700
                                  0.523000
                                                  1.000000
                 -0.704335
                                  0.649137
                                                  1.028697
                                                                  0.066601
                                  0.629924
                 -0.699682
                                                  1.020210
                                                                 0.066379
                 -0.700532
                                  0.634695
                                                  1.021684
                                                                  0.066392
                                  0.633526
                 -0.700347
                                                  1.021322
                                                                  0.066387
                 -0.700393
                                  0.633811
                                                  1.021410
                                                                  0.066388
                 -0.700382
                                  0.633742
                                                  1.021388
                                                                 0.066387
                 -0.700385
                                  0.633759
                                                  1.021393
                                                                 0.066388
                 -0.700384
                                  0.633755
                                                  1.021392
                                                                  0.066388
                 -0.700384
                                  0.633756
                                                  1.021392
                                                                 0.066388
                 -0.700384
                                  0.633755
                                                  1.021392
                                                                  0.066388
        11
                 -0.700384
                                  0.633755
                                                  1.021392
                                                                 0.066388
NOTE: Convergence criterion met.
   Non-Linear Least Squares Summary Statistics
                                                      Dependent Variable COUNT
       Source
                                     Weighted SS
                                                      Weighted MS
       Regression
                                    11.500000000
                                                      3.83333333
       Residual
                                     0.066387556
                                                      0.005532296
       Uncorrected Total
                                    11.566387556
       (Corrected Total)
                              14
                                     0.992150134
       Parameter
                      Estimate
                                   Asymptotic
                                                           Asymptotic 95 %
                                   Std. Error
                                                       Confidence Interval
                                                       Lower
       LOG EC50 -0.700384232 0.04846503062 -.80598061786 -0.594787878558 0.633755386 0.09293379915 0.43126973389 0.8362410382
                  1.021392302 0.04176156192 0.93040154153 1.1123830634
                         Asymptotic Correlation Matrix
        Corr
                           LOG_EC50
                                                  SIGMA
                                                                        CO.
        LOG EC50
                                           -0.138082888
                                                              -0.686018395
           $1 GMA
                       -0.138082888
                                                             0.5815601052
                                          0.5815601052
                       -0.686018395
                             cucumber phytotoxicity
         MODEL: COUNT = CO * PROBNORM ((LOG EC50 - LOG CONC) / SIGMA)
                        SUMMARY OF NONLINEAR REGRESSION
                                                    13:26 Wednesday, May 21, 1997
    \ OBS
            CONC
                     LOG EC50
                                   SIGMA
                                                         RESID SS
                                                                        EC50
                      -0.70038
                                 0.63376
                                             1.02139
                                                         0.066388
                                                                      0.19935
                             cucumber phytotoxicity
```

MODEL: YOUNG = CO \* PROBNORM ((LOG\_EC25 - LOG\_CONC) / SIGMA - 0.67449)

	c.out Page 3					File:/
1.0			·			Error
]	٠					Correc
0.9	Ö	0				
	•••	•				
0.8		····ò				Source
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0.7			•••			Source
0.7		0	••••			DOSE
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0.6			0	•		1
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0.5				•••	0	İ
0.5				•	0	
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0.4					0	
-1.6	-1.4	-1.2	-1.0	-0.8	-0.6	
		. LOG_C	ONC			
NOTE: 932	obs had missing v	values. 851 obs	hidden.		~	
	COMPARISO TEST IF	cucumber phytot ON OF MEANS FOR N TREATMENT IS LE	OEL DETERMINATI SS THAN CONTROL	ON nesday, May	7 21 1997	
	Gene	eral Linear Model		,		
		Class Level Info				}
	Class L	evels Values				
	DOSE	5 0 0.25	0.031 0.062 0.1	24		
	Number o	of observations i	n data set = 30			
	to missing values ysis.	, only 15 observ	ations can be u	sed in this		
		cucumber phytot IN OF MEANS FOR N TREATMENT IS LE	DEL DETERMINATI SS THAN CONTROL	ON nesday, May	8 21, 1997	
•	Gene	eral Linear Model	s Procedure			
Dependent	Variable: RESPONS					
Source	DF	Sum of Squares	Mean Square	f Value	Pr > F	
Model	4	0.64000000	0.16000000	48.00	0.0001	

File:A:cuc.out	Page 4				
Error	10	0.03333333	0.00333333		
Corrected Total	14	0.67333333			
	R-Square	c.v.	Root MSE	RESE	PONSE Mean
	0.950495	7.530656	0.057735		0.766667
Source	DF	Type I \$\$	Mean Square	f Value	Pr > F
DOSE	. 4	0.64000000	0.16000000	48.00	0.0001
Source	DF	Type III SS	Mean Square	f Value	Pr > F
DOSE	4	0.64000000	0.16000000	48.00	0.0001
Į.					

CUCUMBER PHYTOTOXICITY
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL 13:26 Wednesday, May 21, 1997

#### General Linear Models Procedure

Level of		RESPONSE						
DOSE	N	Mean	SD					
0 0.25 0.031 0.062 0.124	3 3 3 3	1.0000000 0.4666667 0.9666667 0.8000000 0.6000000	0.0000000 0.05773503 0.05773503 0.1000000 0.00000000					
0.124	5.10	mbor phytotoxic						

cucumber phytotoxicity
COMPARISON OF MEANS FOR NOEL DETERMINATION TEST IF TREATMENT IS LESS THAN CONTROL
13:26 Wednesday, May 21, 1997

General Linear Models Procedure

Dunnett's One-tailed T tests for variable: RESPONSE

NOTE: This tests controls the type I experimentwise error for comparisons of all treatments against a control.

Alpha= 0.05 Confidence= 0.95 df= 10 MSE= 0.003333 Critical Value of Dunnett's T= 2.466 Minimum Significant Difference= 0.1162

Comparisons significant at the 0.05 level are indicated by '\*\*\*'.

	DOSE Comparison	Simultaneous Lower Confidence Limit	Difference Between Means	Simultaneous Upper Confidence Limit	•
0.	.031 - 0	-0.14956	-0.03333	0.08289	
0.	.062 - 0	-0.31623	-0.20000	-0.08377	***
0.	.124 - 0	-0.51623	-0.40000	-0.28377	***
0	.25 - 0	-0.64956	-0.53333	-0.41711·	***

radish shoot weight

File: rad Transform: NO TRANSFORMATION

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N 	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	10.533	10.533	10.533
2	0.015 lb ai/a	3	9.350	9.350	9.663
3	0.031 lb ai/A	3	9.977	9.977	9.663
4	0.062 lb ai/A	3	8.737	8.737	9.422
5	0.124 lb ai/A	3	9.400	9.400	9.422
6	0.25 lb ai/A	3	10.130	10.130	9.422
l					

radish shoot weight

File: rad Transform: NO TRANSFORMATION

WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2 O	F 2
IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Form. Con. 0.015 lb ai/a 0.031 lb ai/A 0.062 lb ai/A 0.124 lb ai/A 0.25 lb ai/A	10.533 9.663 9.663 9.422 9.422 9.422	1.092 1.092 1.395 1.395 1.395	<del></del> -	1.78 1.87 1.90 1.92 1.93	k= 1, v=12 k= 2, v=12 k= 3, v=12 k= 4, v=12 k= 5, v=12

= 0.976

ote: df used for table values are approximate when v > 20.

NIFL = 0.25 16 ai /A

Soybean phytotoxicity

File: soy Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	1.000	1.412	1.412
2	0.001 lb ai/A	3	1.000	1.412	1.412
3	0.002 lb ai/A	3	1.000	1.412	1.412
4	0.004 lb ai/A	3	0.967	1.358	1.398
5	0.008 lb ai/A	3	1.000	1.412	1.398
6	0.015 lb ai/A	3	1.000	1.412	1.398
7	0.031 lb ai/A	3	1.000	1.412	1.398
8	0.062 lb ai/A	3	0.967	1.358	1.358
9	0.124 lb ai/A	3	0.900	1.249	1.249
10	0.25 lb ai/A	3	0.733	1.030	1.030

Soybean phytotoxicity

. .

File: soy Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2 O	F 2
IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Form. Con. 0.001 lb ai/A 0.002 lb ai/A 0.004 lb ai/A 0.008 lb ai/A 0.015 lb ai/A 0.031 lb ai/A	1.412 1.412 1.412 1.398 1.398 1.398	0.000 0.000 0.353 0.353 0.353		1.72 1.81 1.83 1.85 1.86	k= 1, v=20 k= 2, v=20 k= 3, v=20 k= 4, v=20 k= 5, v=20 k= 6, v=20
0.062 lb ai/A 0.124 lb ai/A 0.25 lb ai/A	1.358 1.249 1.030	1.412 4.236 9.935	* *	1.86 1.87 1.87	k= 7, v=20 k= 8, v=20 k= 9, v=20

0.047

Note: df used for table values are approximate when v > 20.

" NOFE - 0.062 16 a. /A

Sunflower phytotoxicity

Transform: ARC SINE(SQUARE ROOT(Y)) File: sun

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2							
GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN		
1	Form. Con.	3	1.000	1.412	1.412		
2	0.001 lb ai/A	3	0.967	1.358	1.394		
3	0.002 lb ai/A	3	1.000	1.412	1.394		
4	0.004 lb ai/A	·3	1.000	1.412	1.394		
5	0.008 lb ai/A	3	0.967	1.358	1.358		
6	0.015 lb ai/A	3	0.967	1.358	1.358		
7	0.031 lb ai/A	3	0.967	1.358	1.358		
8	0.062 lb ai/A	3	0.933	1.303	1.303		
- 9	0.124 lb ai/A	3	0.600	0.888	0.888		
10	0.25 lb ai/A	3	0.533	0.819	0.819		

Sunflower phytotoxicity

'ile: sun Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2 O	F 2
IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Form. Con. 0.001 lb ai/A 0.002 lb ai/A 0.004 lb ai/A 0.008 lb ai/A 0.015 lb ai/A 0.031 lb ai/A 0.062 lb ai/A	1.412 1.394 1.394 1.358 1.358 1.358 1.358	0.291 0.291 0.291 0.872 0.872 0.872		1.72 1.81 1.83 1.85 1.86 1.86	k= 1, v=20 k= 2, v=20 k= 3, v=20 k= 4, v=20 k= 5, v=20 k= 6, v=20 k= 7, v=20
0.124 lb ai/A 0.25 lb ai/A	0.888	8.420 9.521	*	1.87 1.87	k= 8, v=20 k= 9, v=20

0.076

ote: df used for table values are approximate when v > 20.

NOTEL = 0. 662 16 aila

## sunflower phytotoxicity

### Estimated EC Values and Confidence Limits

Point	Conc.	Lower 95% Confiden	Upper ce Limits
EC 1.00	0.0172		
EC 5.00	0.0368		
EC10.00	0.0553		
EC15.00	0.0727		
EC50.00	0.2313		
EC85.00	0.7358		
EC90.00	0.9676	•	
EC95.00	1.4518		
EC99.00	3.1073		

y = 0,06(x) + 6.31

Figs 6. 104 le a la

tomato shoot weight

File: tom Transform: NO TRANSFORMATION

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	6.843	6.843	6.843
2	0.001 lb ai/A	3	6.017	6.017	6.671
• 3	0.002 lb ai/A	3	6.620	6.620	6.671
4	0.004 lb ai/A	3	6.827	6.827	6.671
5	0.008 lb ai/A	3	6.977	6.977	6.671
6	0.015 lb ai/A	3	6.913	6.913	6.671
7	0.031 lb ai/A	3	5.537	5.537	5.730
- 8	0.062 lb ai/A	3	5.883	5.883	5.730
9	0.124 lb ai/A	3	5.770	5.770	5.730
10	0.25 lb ai/A	3	4.530	4.530	4.530

:omato shoot weight

rile: tom Transform: NO TRANSFORMATION

WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2	OF 2	

IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Form. Con. 0.001 lb ai/A 0.002 lb ai/A 0.004 lb ai/A 0.008 lb ai/A 0.015 lb ai/A 0.031 lb ai/A 0.062 lb ai/A 0.124 lb ai/A 0.25 lb ai/A	6.843 6.671 6.671 6.671 6.671 6.671 5.730 5.730 4.530	0.177 0.177 0.177 0.177 0.177 1.144 1.144 1.144	*	1.72 1.81 1.83 1.85 1.86 1.86 1.86 1.87	k= 1, v=20 k= 2, v=20 k= 3, v=20 k= 4, v=20 k= 5, v=20 k= 6, v=20 k= 7, v=20 k= 8, v=20 k= 9, v=20

<sup>= 1.192</sup> 

NUEL : 0.124 16 1.14

ste: df used for table values are approximate when v > 20.

# tomato shoot weight

# Estimated EC Values and Confidence Limits

Point	Conc.	Lower 95% Confidence	Upper ce Limits
EC 1.00	0.0089		•
EC 5.00	0.0278		
EC10.00	0.0508		
EC15.00	0.0763		
EC50.00	0.4270	`	
EC85.00	2.3898		
EC90.00	3.5918		
EC95.00	6.5689		
EC99.00	20.3812		

Y= 139 1 2 5,51

1675 - C.142 16 a. /A

onion shoot weight

File: oni Transform: NO TRANSFORMATION

	WILLIAMS TEST (Isoto	nic	regression mode	1) TABLE 1 OF	2
GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	1.390	1.390	1.714
2	0.008 lb ai/A	3	1.967	1.967	1.714
3	0.015 lb ai/A	3	1.717	1.717	1.714
4	0.031 lb ai/A	3	1.513	1.513	1.714
5	0.062 lb ai/A	3	1.717	1.717	1.714
6	0.124 lb ai/A	3	1.983	1.983	1.714
7	0.25 lb ai/A	3	1.057	1.057	1.057

orion shoot weight

e: oni Transform: NO TRANSFORMATION

IDENTIFICATION MEA	ONIZED CALC. AN WILLIAMS	SIG TABLE P=.05 WILLIAM	DEGREES OF S FREEDOM
0.008 lb ai/A 1 0.015 lb ai/A 1 0.031 lb ai/A 1 0.062 lb ai/A 1 0.124 lb ai/A 1	1.714 1.714 0.728 1.714 0.728 1.714 0.728 1.714 0.728 1.714 0.728 1.714 0.728	1.76 1.85 1.88 1.89 1.90	k= 1, v=14 k= 2, v=14 k= 3, v=14 k= 4, v=14 k= 5, v=14 k= 6, v=14

<sup>= 0.546</sup> 

NOFEE 6,25 16 4:1A

<sup>&#</sup>x27; 9: df used for table values are approximate when v > 20.

onion height
File: oni2

Transform: NO TRANSFORMATION

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	102.933	102.933	119.317
2	0.008 lb ai/A	3	125.700	125.700	119.317
3	0.015 lb ai/A	3	128.433	128.433	119.317
4	0.031 lb ai/A	3	106.667	106.667	119.317
5	0.062 lb ai/A	3	126.533	126.533	119.317
6	0.124 lb ai/A	3	125.633	125.633	119.317
7	0.25 lb ai/A	3	83.967	83.967	83.967

orion height

I a: oni2 Transform: NO TRANSFORMATION

WILLIAMS TEST (Isotonic regression model) TABLE 2 OF 2

IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Form. Con.	119.317				
0.008 lb ai/A	119.317	0.895		1.76	k = 1, v = 14
0.015 lb ai/A	119.317	0.895		1.85	k = 2, v = 14
0.031 lb ai/A	119.317	0.895		1.88	k = 3, v = 14
0.062 lb ai/A	119.317	0.895		1.89	k = 4, v = 14
0.124 lb ai/A	119.317	0.895		1.90	k = 5, v = 14
0.25 lb ai/A	83.967	1.036		1.91	k = 6, v = 14

s = 22.415

NOTEL: 6,25 16 a. 1A

N  $\ni$ : df used for table values are approximate when v > 20.

Ryegrass phytotoxicity

File: rye Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	1.000	1.412	1.412
2	0.002 lb ai/A	3	1.000	1.412	1.412
3	0.004 lb ai/A	3	1.000	1.412	1.412
4	0.008 lb ai/A	3	1.000	1.412	1.412
5	0.015 lb ai/A	3	1.000	1.412	1.412
6	0.031 lb ai/A	3	1.000	1.412	1.412
7	0.062 lb ai/A	3	0.933	1.310	1.361
8	0.124 lb ai/A	3	1.000	1.412	1.361
9	0.25 lb ai/A	3	0.800	1.116	1.116

Ryegrass phytotoxicity

File: rye Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 2 OF 2

IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Form. Con.	1.412	<del>_</del> _	<b></b>		
0.002 lb ai/A	1.412	0.000		1.73	k = 1, v = 18
0.004 lb ai/A	1.412	0.000		1.82	k = 2, v = 18
0.008 lb ai/A	1.412	0.000		1.85	k = 3, v = 18
0.015 lb ai/A	1.412	0.000		1.86	k = 4, $v = 18$
0.031 lb ai/A	1.412	0.000		1.87	k = 5, v = 18
0.062 lb ai/A	1.361	0.855		1.87	k = 6, $v = 18$
0.124 lb ai/A	1.361	0.855		1.88	k = 7, v = 18
0.25 lb ai/A	1.116	4.984	*	1.88	k = 8, v = 18

s = 0.073

Note: df used for table values are approximate when v > 20.

NOFC - 0. 124 /6 a./A

Date: 5 2 27

17 6 5 7

### DATA EVALUATION RECORD VEGETATIVE VIGOR EC25 TEST § 123-1 (TIER II)

PC Code No.: 128959 1. CHEMICAL: Fluroxypyr

Fluroxypyr methylheptyl ester Purity: 26.9% TEST MATERIAL:

3. CITATION:

> D. Schwab Author:

Title: Evaluating the Effects of Fluroxypyr-MHE

on the Seedling Emergence and Vegetative

Vigor of Non-Target Terrestrial Plants

Study Completion Date: May 7, 1996

ABC Laboratories, Inc., Columbia, MO <u>Laboratory:</u>

DowElanco, Indianapolis, IN Sponsor:

<u>Laboratory Report ID:</u> 42838

MRID No.: 440803-35

D231718 + D7336 845 (sub- - becom) DP Barcode:

Mark Mossler, M.S., Toxicologist, 4. REVIEWED BY:

KBN Engineering and Applied Sciences, Inc.

Signature:

APPROVED BY: Pim Kosalwat, Ph.D., Senior Scientist

KBN Engineering and Applied Sciences, Inc.

P. Kosalwat Date: 6/2/97 Signature:

5. APPROVED BY:

> signature: ( Line Costillo Date: 7/1/97

6. STUDY PARAMETERS:

Definitive Study Duration: 21 days

7. This study is scientifically sound and fulfills CONCLUSIONS: the guideline requirements for a vegetative vigor study with terrestrial plants.

Results Synopsis

Most sensitive monocot: Onion

Most sensitive parameter: phytotoxicity

 $EC_{25}$ : 0.124 lb ai/A NOEL: 0.062 lb ai/A Most sensitive dicot: Cotton

Most sensitive parameter: phytotoxicity

EC<sub>25</sub>: 0.0012 lb ai/A NOEL: 0.0010 lb ai/A

### 8. ADEQUACY OF THE STUDY:

A. Classification: Core.

B. Rationale: N/A.

C. Repairability: N/A.

9. <u>GUIDELINE DEVIATIONS</u>: No guideline deviations of importance

were noted.

### 10. SUBMISSION PURPOSE:

#### 11. MATERIALS AND METHODS:

### A. Test Organisms

Guideline Criteria	Reported Information
Species 6 dicots in 4 families, including soybean and a rootcrop; 4 monocots in 2 families, including corn.	<pre>Dicots: cotton, cucumber, radish, soybean, sunflower, tomato Monocots: corn, onion, ryegrass, wheat</pre>
Number of plants per rep 5	5 (6 for radish)
Source of Seed	Commercial suppliers

#### B. Test System

Guideline Criteria	Reported Information		
Solvent	None .		
Site of test	Greenhouse		
Planting method / type of pot	Planted in 10-cm square pots		
Method of application	Track sprayer		
Method of watering	Hand watered avoiding foliage		

Guideline Criteria	Reported Information
Growth stage at application 1-3 true leaf stage	All plants in either the 2, 3, or 4 leaf stage

# C. Test Design

Guideline Criteria	Reported Information
Dose range 2x or 3x	2x: ranging from 0.55 g active ingredient (ai)/Ha to 280 g ai/Ha (0.0005 - 0.25 lb ai/A)
Doses At least 5	5, 7, 9, or 10
Controls Negative and solvent	Negative (deionized water) and formulation blank controls
Replicates per dose At least 3	3 replicates
Duration of test 14 days	3 weeks
Were observations made at least weekly?	Only "final" rating reported
Maximum labeled rate	280 g ai/Ha (0.25 lb ai/A)

## 12. REPORTED RESULTS:

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes
Was an NOEL observed for each species?	Yes
Phytotoxic observations	Yes
Were initial chemical concentrations measured? (Optional)	Yes, recoveries of selected spray solutions ranged between 97 and 108% of nominal
Were adequate raw data included?	Yes

Results for the most sensitive parameter of each species\*

Species	Parameter	EC <sub>25</sub>	NOEL (g ai/Ha)	
Cotton	phytotoxicity	2.2	1.1	
Cucumber	phytotoxicity	12.8	4.4	
Radish	phytotoxicity	75	35	
Soybean	phytotoxicity	13.1	4.4	
Sunflower	phytotoxicity	3.7	1.1	
Tomato	phytotoxicity	3.8	2.2	
Corn	phytotoxicity	205	35	
Onion	phytotoxicity	248	35	
Ryegrass	all parameters similar	>280	280	
Wheat	phytotoxicity	112	70	

<sup>\*</sup>The most sensitive parameter is based on the EC25 value.

Observations: Symptoms of test material toxicity were mainly manifest as stunting, lodging, leaf wrinkle/rolling, epinasty, and wilting.

<u>Statistical Method</u>: Dunnett's test was used for mean separation using pooled control data for all parameters. Nonlinear least squares regression was employed to determine the EC values.

13. VERIFICATION OF STATISTICAL RESULTS: All comparisons were made against the formulation blank control. Williams' test was used for mean separation. Probit analysis or visual interpretation was used for EC25 determination. The phytotoxic responses of cotton, cucumber, radish, soybean, sunflower, and tomato were remodeled using non-linear regression analysis. All concentrations were converted to lb ai/A before analysis.

Results for the most sensitive parameter of each species

Species	Parameter	EC <sub>25</sub>	NOEL (lb ai/A)
Cotton	phytotoxicity	0.0012	0.0010
Cucumber	phytotoxicity	0.010	0.004
Radish	phytotoxicity	0.056	0.031
Soybean	phytotoxicity	0.008	0.004
Sunflower	phytotoxicity	0.004	0.001
Tomato	phytotoxicity	0.004	0.001
Corn	phytotoxicity	0.176	0.031
Onion	phytotoxicity	0.124	0.062
Ryegrass	all parameters similar	>0.25	0.25
Wheat	phytotoxicity	>0.25	0.062

Results for most sensitive parameter of most sensitive species

	Monocot	Dicot
Species	onion	cotton
Parameter	phytotoxicity	phytotoxicity
EC <sub>25</sub> (lb ai/A)	0.124	0.0012
95% C.I. (lb ai/A)	CNBD*	0.0007 - 0.0020
Probit Slope	N/A	1.2
NOEL (lb ai/A)	0.124	0.031

<sup>\*</sup>CNBD = Could not be determined.

14. REVIEWER'S COMMENTS: The author reported the results in terms of g ai/Ha. The reviewer converted the rates in terms of lb ai/A. This study is scientifically sound and fulfills the guideline requirements. The study is classified as Core.

cotton phytotoxicity

File: cot Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

ROUP	IDENTIFICATION	N 	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	1.000	1.345	1.345
2	0.001 lb ai/A	3	1.000	1.345	1.345
3	0.002 lb ai/A	3	0.767	1.068	1.068
4	0.004 lb ai/A	3	0.500	0.785	0.785
5	0.008 lb ai/A	3	0.333	0.615	0.615
6	0.015 lb ai/A	3	0.267	0.541	0.541
7	0.031 lb ai/A	3	0.200	0.464	0.464
8	0.062 lb ai/A	3	0.100	0.322	0.322
9	0.124 lb ai/A	3	0.100	0.322	0.322
10	0.25 lb ai/A	3	0.100	0.322	0.322

otton phytotoxicity ile: cot Tran Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2	OF	2
---------------	-----------	------------	--------	---------	----	---

IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Form. Con. 0.001 lb ai/A 0.002 lb ai/A 0.004 lb ai/A 0.008 lb ai/A 0.015 lb ai/A 0.031 lb ai/A 0.062 lb ai/A 0.124 lb ai/A 0.25 lb ai/A	1.345 1.345 1.068 0.785 0.615 0.541 0.464 0.322 0.322	0.000 9.513 19.242 25.109 27.642 30.299 35.176 35.176	* * * * * * *	1.72 1.81 1.83 1.85 1.86 1.86 1.86 1.87	k= 1, v=20 k= 2, v=20 k= 3, v=20 k= 4, v=20 k= 5, v=20 k= 6, v=20 k= 7, v=20 k= 8, v=20 k= 9, v=20
					•

NOTE: 0.0016 16 with

ote: df used for table values are approximate when v > 20.

## cotton phyto.

## Estimated EC Values and Confidence Limits

		Lower	Upper
Point	Conc.	95% Confide	nce Limits
EC 1.00	0.0001	0.0000	0.0001
EC 5.00	0.0002	0.0001	0.0004
EC10.00	0.0005	0.0002	0.0008
EC15.00	0.0007	0.0004	0.0011
EC50.00	0.0051	0.0039	0.0063
EC85.00	0.0347	0.0261	0.0510
EC90.00	0.0547	0.0389	0.0880
EC95.00	0.1074	0.0695	0.1989
EC99.00	0.3805	0.2045	0.9306

Y: 1.24(x)+7.85 EC25 0.0014 12 1/A

```
cotton phytotoxicity
                                                                                                                                       15:35 Wednesday, May 21, 1997
                                                  15:35 Wednesday, May 21, 1997
                                                                                                        Non-Linear Least Squares Iterative Phase
       085
               CONC
                       LOG CONC
                                     Y1
                                            Y2
                                                   Y3
                                                                Y5
                                                         Y4
                                                                      Y6
                                                                                                    Dependent Variable COUNT Method: Gauss-Newton
                                                                                           Iter
                                                                                                      LOG EC25
                                                                                                                         SIGMA
                                                                                                                                                 Weighted SS
              0.000
                                    1.0
                                           1.0
                                                                                                      -2.854000
                                                                                                                      0.806000
                                                                                                                                     1,000000
                                                                                                                                                     0.157591
                        -2.69897
              0.002
                                    0.8
                                           0.7
                                                  0.8
                                                                                                      -2.944269
                                                                                                                      0.876367
                                                                                                                                     1.024115
                                                                                                                                                     0.145347
              0.004
                        -2.39794
                                    0.5
                                           0.5
                                                  0.5
                                                                                                      -2.935489
                                                                                                                                     1.020306
                                                                                                                                                     0.145221
                                                                                                                      0.871570
              0.008
                        -2.09691
                                           0.4
                                                  0.3
                                    0.3
                                                                                                      -2.936448
                                                                                                                      0.872149
                                                                                                                                     1.020578
                                                                                                                                                     0.145241
              0.015
                       -1.82391
                                    0.3
                                           0.3
                                                  0.2
                                                                                                      -2.936339
                                                                                                                      0.872083
                                                                                                                                     1.020547
                                                                                                                                                     0.145239
                       -1.50864
              0.031
                                           0.2
                                                  0.2
                                                                                                      -2.936351
                                                                                                                      0.872091
                                                                                                                                      1.020550
                                                                                                                                                     0.145239
                       -1.20761
              0.062
                                    0.1
                                           0.1
                                                  0.1
                                                                                                      -2.936350
                                                                                                                      0.872090
                                                                                                                                      1.020550
                                                                                              6
                                                                                                                                                     0.145239
                             cotton phytotoxicity
                                                                               2
                                                                                                      -2.936350
                                                                                                                      0.872090
                                                                                                                                      1.020550
                                                                                                                                                     0.145239
         MODEL: COUNT = CO * PROBNORM ((LOG EC50 - LOG_CONC) / SIGMA)
                                                                                              8
                                                                                                      -2.936350
                                                                                                                      0.872090
                                                                                                                                     1.020550
                                                                                                                                                     0.145239
                             WEIGHTED REGRESSION
                                                                                     NOTE: Convergence criterion met.
                                                  15:35 Wednesday, May 21, 1997
                   Non-Linear Least Squares Iterative Phase
                                                                                        Non-Linear Least Squares Summary Statistics
                                                                                                                                         Dependent Variable COUNT
               Dependent Variable COUNT Method: Gauss-Newton
      Iter
                 LOG EC50
                                   SIGMA
                                                      CO
                                                            Weighted SS
0.153007
                                                                                                                         Weighted SS
                                                                                            Source
                                                                                                                  DF
                                                                                                                                         Weighted MS
                -2.292000
                                 0.806000
                                                 1.000000
                -2.352710
                                0.876663
                                                1.024334
                                                                0.145246
                                                                                                                        9.5000000000
                                                                                                                                        3.1666666667
                                                                                            Regression
                -2.347616
                                0.871562
                                                1.020302
                                                                0.145221
                                                                                                                        0.1452390498
                                                                                                                   18
                                                                                            Residual
                                                                                                                                        0.0080688361
                -2.348193
                                0.872150
                                                1.020578
                                                                0.145241
                                                                                                                        9.6452390498
                                                                                            Uncorrected Total
                                                                                                                  21
                -2.348127
                                0.872083
                                                1.020547
                                                                0.145239
                -2.348135
                                0.872091
                                                1.020550
                                                                0.145239
                                                                                            (Corrected Total)
                                                                                                                  20
                                                                                                                        4.0243436896
                -2.348134
                                0.872090
                                                1.020550
                                                                0.145239
                -2.348134
                                0.872090
                                                1.020550
                                                                0.145239
                -2.348134
                                0.872090
                                                1.020550
                                                                0.145239
                                                                                            Parameter
                                                                                                          Estimate
                                                                                                                       Asymptotic
                                                                                                                                               Asymptotic 95 %
NOTE: Convergence criterion met.
                                                                                                                       Std. Error
                                                                                                                                           Confidence Interval
                                                                                                                                           Lower
                                                                                            LOG EC25 -2.936349898 0.10980214469 -3.1670341193 -2.7056656761
  Non-Linear Least Squares Summary Statistics
                                                    Dependent Variable COUNT
                                                                                               SIGMA
                                                                                                       0.872089781 0.06660069536 0.7321678368 1.0120117252
                                                                                                       1.020549769 0.05184546698 0.9116272040 1.1294723330
       Source
                                    Weighted SS
                                                    Weighted MS
       Regression
                                  9.5000000000
                                                   3.1666666667
                                                                                                             Asymptotic Correlation Matrix
       Residual
                                  0.1452390498
                                                   0.0080688361
      Uncorrected Total
                             21
                                  9.6452390498
                                                                                             Corr
                                                                                                               LOG EC25
                                                                                                                                     SIGMA
                                                                                                                                                           CO
       (Corrected Total)
                             20
                                  4.0243436897
                                                                                             LOG EC25
                                                                                                                                                 -0.705759552
                                                                                                                              -0.890572698
                                                                                                SIGMA
                                                                                                            -0.890572698
                                                                                                                                                 0.4394570461
                                                                                                   C0
                                                                                                            -0.705759552
                                                                                                                              0.4394570461
       Parameter
                     Estimate
                                  Asymptotic
                                                         Asymptotic 95 %
                                                                                                                   cotton phytotoxicity
                                  Std. Error
                                                     Confidence Interval
                                                                                         MODEL: YOUNG = CO * PROBNORM ((LOG EC25 - LOG CONC) / SIGMA - 0.67449)
                                                                                                            SUMMARY OF NONLTHEAR REGRESSION
                                                      Lower
       LOG EC50
                 -2.348134061 0.07272546353 -2.5009235809 -2.1953445417
                                                                                                                                        15:35 Wednesday, May 21, 1997
          51GMA
                  0.872089781 0.06660069536 0.7321678367 1.0120117252
                  1.020549768 0.05184546698 0.9116272039 1.1294723330
                                                                                                CONC
                                                                                         OBS
                                                                                                        LOG EC25
                                                                                                                      SIGMA
                                                                                                                                   CO
                                                                                                                                                          EC25
                                                                                                                                            RESID_SS
                                                                                          1
                                                                                                         -2.93635
                                                                                                                     0.87209
                                                                                                                                1.02055
                                                                                                                                             0.14524
                                                                                                                                                         .0011578
                        Asymptotic Correlation Matrix
                                                                                                                   cotton phytotoxicity
                                                                                         MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
                          LOG EC50
        Corr
                                                SIGMA
                                                                      CO
                                                                                                                                       T5:35 Wednesday, May 21, 1997
        LOG EC50
                                          -0.72691581
                                                            -0.794121324
                                                                                                      Plot of COUNT*LOG CONC. Symbol used is '0'.
                        -0.72691581
                                                            0.4394570461
           SIGMA
                                                                                                      Plot of PRED*LOG CONC.
                                                                                                                                Symbol used is '.'.
              CO
                       -0.794121324
                                         0.4394570461
                                                                                3
                              cotton phytotoxicity
                                                                                     COUNT
         MODEL: COUNT = CO * PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
                       SUMMARY OF NONLINEAR REGRESSION
                                                                                       1.2
                                                  15:35 Wednesday, May 21, 1997
           CONC
                   LOG EC50
   OBS
                                 SIGMA
                                              C0
                                                       RESID SS
                                                                     EC50
                    -2.34813
                               0.87209
                                          1.02055
                                                       0.14524
                                                                    .0044861
    cotton phylotoxicity

MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
                                                                                       1.0
                             WEIGHTED REGRESSION
```

|File:a:cot.out Page 2

|File:a:cot.out Page 1

```
|File:a:cot.out Page 3
  0.8.0
        0
  0.6
  0.2
  0.0
     -2.75
                -2.50
                          -2.25
                                    -2.00
                                              -1.75
                                                        -1.50
                                                                  -1.25
                                                                          -1.00
                                       LOG CONC
NOTE: 1522 obs had missing values. 1462 obs hidden.
                                                                              7
                             cotton phytotoxicity
                  COMPARISON OF MEANS FOR NOEL DETERMINATION
                    TEST IF TREATMENT IS LESS THAN CONTROL
                                                  15:35 Wednesday, May 21, 1997
                        General Linear Models Procedure
                           Class Level Information
           Class
                    Levels
                              Values
                              0 0.002 0.004 0.008 0.015 0.031 0.062
           DOSE
                   Number of observations in data set = 42
NOTE: Due to missing values, only 21 observations can be used in this
      analysis.
                                                                              8
                             cotton phytotoxicity
                  COMPARISON OF MEANS FOR NOEL DETERMINATION
                    TEST IF TREATMENT IS LESS THAN CONTROL
                                                 15:35 Wednesday, May 21, 1997
                       General Linear Models Procedure
Dependent Variable: RESPONSE
                                    Sum of
                                                      Mean
                                   Squares
Source
                                                             F Value
                                                                         Pr > F
                                                    Square
                                1.91238095
                                                                         0.0001
Model
                                                0.31873016
                         6
                                                              223.11
Error
                        14
                                0.02000000
                                                0.00142857
```

File:a:cot.out Corrected Total	Page 4 20	1.93238095			
	R-Square	c.v.	Root MSE	RESI	PONSE Mean
	0.989650	8.355004	0.037796		0.452381
Source	DF	Type I \$\$	Mean Square	F Válue	Pr > F
DOSE	6	1.91238095	0.31873016	223.11	0.0001
Source	DF	Type III SS	Mean Square	F Value	Pr > F
DOSE	6	1.91238095	0.31873016	223.11	0.0001

cotton phytotoxicity 9
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL
15:35 Wednesday, May 21, 1997

#### General Linear Models Procedure

Level of	evel ofRESPONSE				
DOSE	N	Mean	, SD		
0 0.002 0.004 0.008 0.015 0.031	3 3 3 3 3	1.0000000 0.7666667 0.50000000 0.33333333 0.2666667 0.2000000	0.0000000 0.05773503 0.00000000 0.05773503 0.05773503 0.00000000		
0.062	3	0.10000000	0.0000000		
	CO	tton phytotoxici1	ty		
COMPARIS	SON OF	MEAN'S FOR NOEL D	DETERMINATION		
TEST	IF TOF	ATMENT IS LESS TH	IAN CONTROL		

General Linear Models Procedure

Dunnett's One-tailed T tests for variable: RESPONSE

NOTE: This tests controls the type I experimentwise error for comparisons of all treatments against a control.

Alpha= 0.05 Confidence= 0.95 df= 14 MSE= 0.001429 Critical Value of Dunnett's T= 2.532 Minimum Significant Difference= 0.0781

Comparisons significant at the 0.05 level are indicated by '\*\*\*'.

DOSE Comparison	Simultaneous Lower Confidence Limit	Difference Between Means	Simultaneous Upper Confidence Limit	<b>;</b>
0.002 - 0	-0.31148	-0.23333	-0.15519	***
0.004 - 0	-0.57815	-0.50000	-0.42185	***
0.008 - 0	-0.74481	-0.66667	-0.58852	***
0.015 - 0	-0.81148	-0.73333	-0.65519	***
0.031 - 0	-0.87815	-0.80000	-0.72185	***
0.062 - 0	-0.97815	-0.90000	-0.82185	***

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15:35 Wednesday, May 21, 1997

cucumber phytotoxicity

File: cuc Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N 	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	1.000	1.345	1.345
2	0.001 lb ai/A	3	1.000	1.345	1.345
3	0.002 lb ai/A	٦3	1.000	1.345	1.345
4	0.004 lb ai/A	3	1.000	. 1.345	1.345
5	0.008 lb ai/A	3	0.767	1.068	1.068
6	0.015 lb ai/A	3	0.633	0.921	0.921
7	0.031 lb ai/A	3	0.467	0.752	0.752
8	0.062 lb ai/A	3	0.300	0.580	0.580
9	0.124 lb ai/A	3	0.067	0.290	0.290
10	0.25 lb ai/A	3	0.000	0.226	0.226

ucumber phytotoxicity

'ile: cuc Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 2 OF 2

IDENTIFICATION	ISOTONIZED	CALC.	SIG	TABLE	DEGREES OF
	MEAN	WILLIAMS	P=.05	WILLIAMS	FREEDOM
Form. Con. 0.001 lb ai/A	1.345 1.345	0.000		1.72	k= 1, v=20
0.002 lb ai/A	1.345	0.000		1.81	k = 2, v = 20
0.004 lb ai/A	1.345	0.000	*	1.83	k= 3, v=20
0.008 lb ai/A	1.068	8.872		1.85	k= 4, v=20
0.015 lb ai/A	0.921	13.596	*	1.86	k= 5, v=20
0.031 lb ai/A	0.752	19.022		1.86	k= 6, v=20
0.062 lb ai/A	0.580	24.541	*	1.86	k = 7, v = 20
0.124 lb ai/A	0.290	33.836	*	1.87	k= 8, v=20
0.25 lb ai/A	0.226	35.892		1.87	k= 9, v=20

= .0.038

ote: df used for table values are approximate when v > 20.

NOFE = 0.004 15 a-/2

21/6

cucumber phyto.

Estimated EC Values and Confidence Limits

Point	Conc.	Lower 95% Confider	Upper ace Limits
EC 1.00	0.0010	0.0005	0.0017
EC 5.00	0.0026	0.0015	0.0038
EC10.00	0.0042	0.0027	0.0059
EC15.00	0.0059	0.0040	0.0079
EC50.00	0.0245	0.0206	0.0289
EC85.00	0.1012	0.0790	0.1413
EC90.00	0.1416	0.1060	0.2109
EC95.00	0.2329	0.1631	0.3835
EC99.00	0.5920	0.3629	1.1863

Y = 1.68(x)+ 7.71

El25 C. C. C. C. 16 21/A

9911

```
File:a:cuc.out Page 1
                                                                                   cucumber phytotoxicity
                                                                                                       -1.55285
                                                                                                                 0.51733 0.95735
                                                                                                                                          0.20077
                                                                                                                                                      0.027999
                                                                                                0
                                                  15:35 Wednesday, May 21, 1997
                                                                                                                cucumber phytotoxicity
                                                                                        MODEL: YOUNG = CO * PROBNORM ((LOG EC25 - LOG_CONC) / SIGMA - 0.67449)
       OBS
               CONC
                       LOG CONC
                                    Y1
                                           Y2
                                                  Y3
                                                         Y4
                                                              Y5
                                                                     Y6
                                                                                                                 WEIGHTED REGRESSION
                                                                                                                                      15:35 Wednesday, May 21, 1997
              0.000
                                   1 0
                                          1.0
              0.008
                       -2.09691
                                   0.8
                                          0.7
                                                 0.8
                                                                                                       Non-Linear Least Squares Iterative Phase
              0.015
                       -1.82391
                                   0.7
                                          0.6
                                                 0.6
                                                                                                   Dependent Variable COUNT Method: Gauss-Newton
              0.031
                       -1.50864
                                          0.5
                                                 0.5
                                   0.4
                                                                                                     LOG EC25
                                                                                         lter
                                                                                                                       SIGMA
                                                                                                                                               Weighted SS
              0.062
                       -1.20761
                                   0.3
                                          0.3
                                                 0.3
                                                                                                    -2.0T2000
                                                                                                                    0.595000
                                                                                                                                   1.000000
0.968703
                                                                                                                                                   0.200753
                                                                                                    -1.923815
              0.124
                       -0.90658
                                                                                                                    0.530760
                                   0.0
                                          0.1
                                                 0.1
                                                                                                                                                   0.199013
        cucumber phytotoxicity

MODEL: COUNT = CO * PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
                                                                                                    -1.907395
                                                                             12
                                                                                                                    0.520751
                                                                                                                                   0.959933
                                                                                                                                                   0.200273
                                                                                                    -1.903269
                                                                                                                    0.518227
                                                                                                                                   0.958038
                                                                                                                                                   0.200636
                             WEIGHTED REGRESSION
                                                                                                                    0.517567
                                                                                                                                   0.957534
                                                                                                    -1.902180
                                                                                                                                                   0.200735
                                                 15:35 Wednesday, May 21, 1997
                                                                                                    -1.901890
                                                                                                                    0.517392
                                                                                                                                   0.957400
                                                                                                                                                   0.200761
                                                                                                    -1.901813
                                                                                                                    0.517345
                                                                                                                                    0.957365
                                                                                                                                                   0.200768
                   Non-Linear Least Squares Iterative Phase
                                                                                                                    0.517333
                                                                                                    -1.901792
                                                                                                                                   0.957355
                                                                                                                                                   0.200770
              Dependent Variable COUNT Method: Gauss-Newton
                                                                                                    -1.901787
                                                                                                                    0.517330
                                                                                                                                   0.957353
                                                                                                                                                   0.200771
                LOG EC50
     Iter
                                   SIGMA
                                                           Weighted SS
                                                                                                    -1.901785
                                                                                                                    0.517329
                                                                                                                                   0.957352
                                                                                                                                                   0.200771
                -1.6T1000
                                0.595000
                                               1.000000
                                                              0.200895
                                                                                            10
                                                                                                    -1.901785
                                                                                                                    0.517328
                                                                                                                                   0.957352
                                                                                                                                                   0.200771
                -1.565821
                                0.530781
                                               0.968710
                                                              0.199003
                                                                                            11
                                                                                                    -1.901785
                                                                                                                    0.517328
                                                                                                                                   0.957352
                                                                                                                                                   0.200771
                -1.556157
                                0.520754
                                               0.959936
                                                              0.200272
                                                                                            12
                                                                                                    -1.901785
                                                                                                                    0.517328
                                                                                                                                   0.957352
                                                                                                                                                   0.200771
                                0.518228
                -1.553731
                                               0.958038
                                                              0.200636
                                                                                            13
                                                                                                    -1.901785
                                                                                                                    0.517328
                                                                                                                                    0.957352
                                                                                                                                                   0.200771
                -1.553086
                                0.517568
                                                              0.200735
                                               0.957535
                                                                                   NOTE: Convergence criterion met.
                -1.552915
                                0.517392
                                               0.957400
                                                              0.200761
                -1.552869
                                0.517345
                                               0.957365
                                                              0.200768
                -1.552856
-1.552853
                                0.517333
                                               0.957355
                                                              0.200770
                                                                                       Non-Linear Least Squares Summary Statistics
                                                                                                                                       Dependent Variable COUNT
                                0.517330
                                               0.957353
                                                              0.200771
                -1.552852
                                0.517329
                                               0.957352
                                                              0.200771
                                                                                           Source
                                                                                                                       Weighted SS
                                                                                                                                        Weighted MS
                                               0.957352
        10
                -1.552852
                                0.517328
                                                              0.200771
        11
                -1.552852
                                0.517328
                                               0.957352
                                                              0.200771
                                                                                           Regression
                                                                                                                      9.7000000000
        12
                                0.517328
                -1.552852
                                               0.957352
                                                              0.200771
                                                                                           Residual
                                                                                                                      0.2007708089
                                                                                                                                       0.0133847206
        13
                -1.552852
                                0.517328
                                               0.957352
                                                              0.200771
                                                                                           Uncorrected Total
                                                                                                                      9.9007708089
                                                                                                                 18
NOTE: Convergence criterion met.
                                                                                                                 17 4.7284710768
                                                                                           (Corrected Total)
  Non-Linear Least Squares Summary Statistics
                                                   Dependent Variable COUNT
                                                                                           Parameter
                                                                                                         Estimate
                                                                                                                     Asymptotic
                                                                                                                                            Asymptotic 95 %
       Source
                                   Weighted SS
                                                    Weighted MS
                                                                                                                     Std. Error
                                                                                                                                         Confidence Interval
                                                                                                                                         Lower
      Regression
                                  9.7000000000
                                                  3.2333333333
                                                                                          LOG EC25 -1.901784756 0.09488565004 -2.1040279626 -1.6995415490
      Residual
                             15
                                  0.2007708089
                                                  0.0133847206
                                                                                             $IGMA 0.517328349 0.05724137514 0.3953217101 0.6393349885
      Uncorrected Total
                                  9.9007708089
                                                                                                     0.957351595 0.06136026168 0.8265657901 1.0881373994
       (Corrected Total)
                             17 4.7284710768
                                                                                                            Asymptotic Correlation Matrix
      Parameter
                     Estimate
                                 Asymptotic
                                                        Asymptotic 95 %
                                                                                           Corr
                                                                                                              LOG_EC25
                                                                                                                                    SIGMA
                                                                                                                                                         CO
                                 Std. Error
                                                    Confidence Interval
                                                    Lower
                                                                   Upper
                                                                                           LOG EC25
                                                                                                                             -0.886668143
                                                                                                                                               -0.776365242
      LOG_EC50 -1.552851957 0.06322542518 -1.6876132489 -1.4180906660
                                                                                                          -0.886668143
                                                                                               SIGMA
                                                                                                                                               0.5738358563
         SIGMA 0.517328349 0.05724137514 0.3953217101 0.6393349885
                                                                                                          -0.776365242
                                                                                                                            0.5738358563
            CO 0.957351595 0.06136026168 0.8265657901 1.0881373994
                                                                                                                cucumber phytotoxicity
                                                                                       MODEL: YOUNG = CO * PROBNORM ((LOG EC25 - LOG CONC) / SIGMA - 0.67449)
SUMMARY OF NONLTNEAR REGRESSION
                        Asymptotic Correlation Matrix
                                                                                                                                      15:35 Wednesday, May 21, 1997
       Corr
                         LOG EC50
                                               SIGMA
                                                                                       OBS
                                                                                               CONC
                                                                                                       LOG EC25
                                                                                                                                          RESID SS
                                                                                                                                                        EC25
       LOG EC50
                                         -0.720016478
                                                           -0.814717243
                                                                                                       -1.90178
                                                                                                                   0.51733
                                                                                                                              0.95735
                                                                                                                                           0.20077
                                                                                                                                                      0.012538
          51GMA
                      -0.720016478
                                                           0.5738358563
                                                                                                                cucumber phytotoxicity
                      -0.814717243
                                        0.5738358563
                                                                                        MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
                            cucumber phytotoxicity
                                                                             13
                                                                                                                                      T5:35 Wednesday, May 21, 1997
         MODEL: COUNT = CO * PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
                       SUMMARY OF NONLINEAR REGRESSION
                                                                                                     Plot of COUNT*LOG CONC. Symbol used is '0'.
                                                 15:35 Wednesday, May 21, 1997
                                                                                                     Plot of PRED*LOG CONC. Symbol used is '.'.
... OBS
          CONC
                  LOG EC50
                                SIGMA
                                             C0
                                                     RESID SS
                                                                    EC50
                                                                                   COUNT
```

```
|File:a:cuc.out Page 3
   1.0
   0.8
            0....
   0.6
   0.4
   0.2
                                                                         ..0
  0.0
                                                                           0
      -2.2
                 -2.0
                           -1.8
                                     -1.6
                                                -1.4
                                                          -1.2
                                                                    -1.0
                                                                              -0.8
                                        LOG CONC
NOTE: 1218 obs had missing values. 1147 obs hidden.
                   CUCUMBER PHYLOTOXICITY
COMPARISON OF MEANS FOR NOEL DETERMINATION
                                                                                17
                     TEST IF TREATMENT IS LESS THAN CONTROL
                                                   15:35 Wednesday, May 21, 1997
                        General Linear Models Procedure
                            Class Level Information
               Class
                        Levels
                                   Values
               DOSE
                                   0 0.008 0.015 0.031 0.062 0.124
                    Number of observations in data set = 36
NOTE: Due to missing values, only 18 observations can be used in this
       analysis.
                              cucumber phytotoxicity
                                                                                18
                   COMPARISON OF MEANS FOR NOEL DETERMINATION
                     TEST IF TREATMENT IS LESS THAN CONTROL
                                                   15:35 Wednesday, May 21, 1997
                        General Linear Models Procedure
Dependent Variable: RESPONSE
                                      Sum of
                                                        Mean
Source
                                     Squares
                                                      Square
                                                               F Value
                                                                            Pr > F
Model
                          5
                                  1.67611111
                                                 0.33522222
                                                                150.85
                                                                            0.0001
```

File:a:cuc.out	Page 4				
Error	12	0.02666667	0.00222222		
Corrected Total	17	1.70277778			
	R-Square	c.v.	Root MSE	RESI	PONSE Mean
	0.984339	8.747713	0.047140		0.538889
Source	DF	Type I SS	Mean Square	F Value	Pr > F
DOSE	5	1.67611111	0.33522222	150.85	0.0001
Source	DF	Type III SS	Mean Square	F Value	Pr > f
DOSE	5	1.67611111	0.33522222	150.85	0.0001

CUCUMBER Phytotoxicity . 19
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL
15:35 Wednesday, May 21, 1997

#### General Linear Models Procedure

Level ofRESPONSE				
DOSE	N	Mean	SD	
0 0.008 0.015 0.031 0.062	3 3 3 3	1.00000000 0.7666667 0.6333333 0.4666667 0.3000000	0.00000000 0.05773503 0.05773503 0.05773503 0.00000000	·
0.124	ž	0.06666667	0.05773503	
	SON OF	mber phytotoxic MEANS FOR NOEL	DETERMINATION	20
TEST	IF TREA	TMENT IS LESS T	HAN CONTROL 15:35 Wednesday,	May 21, 1997

#### General Linear Models Procedure

Dunnett's One-tailed T tests for variable: RESPONSE

NOTE: This tests controls the type I experimentwise error for comparisons of all treatments against a control.

Alpha= 0.05 Confidence= 0.95 df= 12 MSE= 0.002222 Critical Value of Dunnett's T= 2.502 Minimum Significant Difference= 0.0963

Comparisons significant at the 0.05 level are indicated by '\*\*\*'.

DOSE Comparison	Simultaneous Lower Confidence Limit	Difference Between Means	Simultaneous Upper Confidence Limit	6
0.008 - 0	-0.32964	-0.23333	-0.13703	***
0.015 - 0	-0.46297	-0.36667	-0.27036	
0.031 - 0	-0.62964	-0.53333	-0.43703	
0.062 - 0	-0.79631	-0.70000	-0.60369	
0.124 - 0	-1.02964	-0.93333	-0.83703	

adish phytotoxicity

ile: rad Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

ROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1 2 3 4 5	Form. Con. 0.015 lb ai/A 0.031 lb ai/A 0.062 lb ai/A 0.124 lb ai/A 0.25 lb ai/A	3 3 3 3 3	1.000 1.000 0.967 0.733 0.500 0.300	1.365 1.365 1.327 1.033 0.785 0.580	1.365 1.365 1.327 1.033 0.785 0.580

adish phytotoxicity

i'e: rad Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 2 OF 2

IDENTIFICATION	ISOTONIZED	CALC.	SIG	TABLE	DEGREES OF
	MEAN	WILLIAMS	P=.05	WILLIAMS	FREEDOM
Form. Con. 0.015 lb ai/A 0.031 lb ai/A 0.062 lb ai/A 0.124 lb ai/A 0.25 lb ai/A	1.365 1.365 1.327 1.033 0.785 0.580	0.000 0.805 6.898 12.055 16.333	* * *	1.78 1.87 1.90 1.92	k= 1, v=12 k= 2, v=12 k= 3, v=12 k= 4, v=12 k= 5, v=12

0.059

te: df used for table values are approximate when v > 20.

NIEL C. C. 131 16 m. /a

radish phyto.

### Estimated EC Values and Confidence Limits

		Lower	Upper
Point	Conc.	95% Confidence Limits	
EC 1.00	0.0074	0.0019	0.0151
EC 5.00	0.0171	0.0064	0.0285
EC10.00	0.0267	0.0123	0.0402
EC15.00	0.0361	0.0191	0.0509
EC50.00	0.1287	0.1066	0.1564
EC85.00	0.4590	0.3215	0.8899
EC90.00	0.6201	0.4062	1.3798
EC95.00	0.9684	0.5724	2.6518
EC99.00	2.2343	1.0836	9.0766

Y= 135(x)+6.67

EC2- C. 057 11 a. /A

•.

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|File:a:rad.out Page 1
                                                                                   ||File:a:rad.out | Page 2
                              radish phytotoxicity
                                                                             21
                                                                                                    -1.254707
                                                                                                                    0.538342
                                                                                                                                   1.002204
                                                                                                                                                   0.038380
                                                  15:35 Wednesday, May 21, 1997
                                                                                                    -1.254550
                                                                                                                    0.538171
                                                                                                                                   1.002136
                                                                                                                                                   0.038378
                                                                                                                    0.538175
                                                                                                                                   1.002138
                                                                                                    -1.254554
                                                                                                                                                   0.038378
       OBS
               CONC
                       LOG CONC
                                    Y1
                                            Y2
                                                   Y3
                                                               Y5
                                                                                                    -1.254554
                                                                                                                    0.538175
                                                                                                                                   1.002138
                                                                                                                                                   0.038378
                                                                     Y6
                                                                                                    -1.254554
                                                                                                                    0.538175
                                                                                                                                   1.002138
                                                                                                                                                   0.038378
              0.000
                                   1.0
                                           1.0
                                                  1.0
                                                                                    NOTE: Convergence criterion met.
                       -1.20761
              0.062
                                          0.6
                                   0.8
                                                  0.8
              0.124
                       -0.90658
                                          0.5
                                   0.5
                                                  0.5
              0.250
                       -0.60206
                                          0.3
                                   0.3
                                                  0.3
                                                                                                                                       Dependent Variable COUNT
                                                                                       Non-Linear Least Squares Summary Statistics
         redish phytotoxicity

MODEL: COUNT = CO * PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
                                                                             22
                                                                                           Source
                                                                                                                       Weighted SS
                                                                                                                                        Weighted MS
                             WEIGHTED REGRESSION
                                                  15:35 Wednesday, May 21, 1997
                                                                                                                      7.6000000000
                                                                                                                                       2.5333333333
                                                                                           Regression
                                                                                                                      0.0383782402
                                                                                                                                       0.0042642489
                                                                                           Residual
                   Non-Linear Least Squares Iterative Phase
                                                                                           Uncorrected Total
                                                                                                                 12
                                                                                                                      7.6383782402
               Dependent Variable COUNT Method: Gauss-Newton
      Iter
                 LOG EC50
                                   SIGMA
                                                     CO.
                                                           Weighted SS
                                                                                           (Corrected Total)
                                                                                                                 11
                                                                                                                      1.4083914635
                -0.890000
                                0.532000
                                                1.000000
                                                               0.038350
                -0.891615
                                0.538282
                                                1.002193
                                                               0.038380
                -0.891559
                                0.538172
                                                1.002137
                                                               0.038378
                                                                                           Parameter
                                                                                                         Estimate
                                                                                                                     Asymptotic
                                                                                                                                             Asymptotic 95 %
                -0.891560
                                0.538175
                                                1.002138
                                                               0.038378
                                                                                                                     Std. Error
                                                                                                                                         Confidence Interval
                -0.891560
                                0.538175
                                                1.002138
                                                               0.038378
                                                                                                                                         Lower
                -0.891560
                                0.538175
                                                1.002138
                                                               0.038378
                                                                                           LOG EC25 -1.254554211 0.06335136466 -1.3978661736 -1.1112422482
NOTE: Convergence criterion met.
                                                                                              SIGMA
                                                                                                      0.538175145 0.05583572651 0.4118648818 0.6644854086
                                                                                                     1.002137952 0.03756898726 0.9171502750 1.0871256285
   Non-Linear Least Squares Summary Statistics
                                                 Dependent Variable COUNT
                                                                                                            Asymptotic Correlation Matrix
       Source
                                   Weighted SS
                                                    Weighted MS
                                                                                            Corr
                                                                                                              LOG EC25
                                                                                                                                   SIGMA
       Regression
                                  7.6000000000
                                                   2.5333333333
                                  0.0383782402
       Residual
                                                   0.0042642489
                                                                                            LOG EC25
                                                                                                                             -0.866123807
                                                                                                                                               -0.672059919
       Uncorrected Total
                             12
                                  7.6383782402
                                                                                               SIGMA
                                                                                                          -0.866123807
                                                                                                                                               0.3890831283
                                                                                                  C0
                                                                                                          -0.672059919
                                                                                                                            0.3890831283
                             11 1.4083914635
       (Corrected Total)
                                                                                                                 radish phytotoxicity
                                                                                        MODEL: YOUNG = CO * PROBNORM ((LOG EC25 - LOG CONC) / SIGMA - 0.67449)
                                                                                                           SUMMARY OF NONLTHEAR REGRESSION
       Parameter
                     Estimate
                                 Asymptotic
                                                        Asymptotic 95 %
                                                                                                                                      15:35 Wednesday, May 21, 1997
                                 Std. Error
                                                     Confidence Interval
                                                     Lower
                                                                                        OBS
                                                                                               CONC
                                                                                                       LOG_EC25
                                                                                                                    SIGMA
                                                                                                                                          RESID SS
                                                                                                                                                        EC25
       LOG EC50 -0.891560457 0.03603930048 -.97308771265 -0.8100332018
                 0.538175145 0.05583572651 0.41186488180 0.6644854086
          SIGMA
                                                                                         1
                                                                                                 0
                                                                                                       -1.25455
                                                                                                                   0.53818
                                                                                                                              1.00214
                                                                                                                                          0.038378
                                                                                                                                                      0.055648
             CO 1.002137952 0.03756898726 0.91715027498 1.0871256285
                                                                                                                 radish phytotoxicity
                                                                                        MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
                                                                                                                                      T5:35 Wednesday, May 21, 1997
                        Asymptotic Correlation Matrix
                                                                                                     Plot of COUNT*LOG CONC. Symbol used is '0'.
        Corr
                          LOG_EC50
                                               SIGMA
                                                                     C0
                                                                                                     Plot of PRED*LOG CONC. Symbol used is '.'.
        LOG EC50
                                         -0.477519977
                                                           -0.774787339
                                                                                    COUNT
                      -0.477519977
           SIGMA
                                                           0.3890831283
                                         0.3890831283
                       -0.774787339
                                                                                      1.0
                             radish phytotoxicity
                                                                             23
         MODEL: COUNT = CO * PROBNORM ((LOG EC50 - LOG CONC) / SIGMA)
                       SUMMARY OF NONLINEAR REGRESSION
                                                  15:35 Wednesday, May 21, 1997
                                                                                      0.9
     OBS
            CONC
                    LOG EC50
                                 SIGMA
                                               CO
                                                                     EC50
                                                       RESID SS
 :\ 1
              0
                    -0.89156
                                0.53818
                                          1.00214
                                                       0.038378
                                                                   0.12836
                             radish phytotoxicity
    MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
                                                                                      0.8
                             WEIGHTED REGRESSION
                                                  15:35 Wednesday, May 21, 1997
                   Non-Linear Least Squares Iterative Phase
               Dependent Variable COUNT Method: Gauss-Newton
                                                                                      0.7
                 LOG EC25
                                  SIGMA
      Iter
                                                      C0
                                                            Weighted SS
                 -1.245000
                                               1.000000
                                0.532000
                                                               0.038307
```

[File:a:rad.out	Page 3				
11100000	, age 5				
0.6	1				
		••••			
		•••			
0.5		•	·		
			••••		
			••••		
0.4			• ,	••••	
			•		
•				••••	••
0.3					0
-1.3 -	1.2 -1.1	-1.0	-0.9 -0.8	-0.7	-0.6
		rog_co	NC		
NOTE: 628 obs ha	d missing val	ues. 549 obs h	idden.		27
		radish phytotox OF MEANS FOR NO	EL DÉTERMINATIO	ON .	27
	TEST IF T	REATMENT IS LES		nesday, May	21. 1997
	Cononn	l Lincom Madala		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	<b>-</b> 7, 1771
		l Linear Models ass Level Infor			
	Class	Levels Value	s		
	DOSE	4 0 0.2	5 0.062 0.124		
	Number of	observations in	data set = 24		
NOTE: Due to mis analysis.	sing values,	only 12 observa	tions can be u	sed in this	
•		radish phytotox	icity		28
		OF MEANS FOR NO	EL DÉTERMINATIO	ON	
	1E31 IF 1	REATMENT IS LES		nesday, May	21, 1997
	Genera	l Linear Models	Procedure		
Dependent Variab	le: RESPONSE				
Source	DF	Sum of Squares	Mean Square	f Value	Pr > f
Model	3	0.82000000	0.27333333	82.00	0.0001
Error	8	0.02666667	0.00333333		
Corrected Total	11	0.84666667			
	R-Square	c.v.	Root MSE	RESPO	NSE Mean
·	0.968504	9.116057	0.057735		0.633333
Source	DF	Type I SS	Mean Square	F Value	Pr > F

DOSE

3

0.82000000

0.27333333

82.00

0.0001

File:a:rad.out	Page 4				
Source	DF	Type III \$\$	Mean Square	F Value	Pr > f
DOSE	3	0.82000000	0.27333333	82.00	0.0001
		radish phytoto; ON OF MEANS FOR NO F TREATMENT IS LES	DEL DETERMINATIO SS THAN CONTROL	ON nesday, May	29 21, 1997
	Gene	eral Linear Models	Procedure		
	Level of DOSE	N Mean	RESPONSESD		
	0 0.25 0.062 0.124	3 1.00000000 3 0.30000000 3 0.73333333 3 0.5000000	0.000000 0.115470	000 005	
	COMPARISO	radish phytoto ON OF MEANS FOR NO F TREATMENT IS LES	cicity DEL DETERMINATIONS THAN CONTROL	DN nesday, May	30 21. 1997
	Gene	eral Linear Models		,,,	
Du	ınnett's One	-tailed T tests fo	or variable: RES	SPONSE	
NOTE:	This tests of comparisons	controls the type of all treatments	I experimentwis against a conf	se error fo trol.	r

Alpha= 0.05 Confidence= 0.95 df= 8 MSE= 0.003333 Critical Value of Dunnett's T= 2.416 Minimum Significant Difference= 0.1139

Comparisons significant at the 0.05 level are indicated by  $^{\prime***\prime}$ .

DOSE Comparison	Simultaneous Lower Confidence Limit	Difference Between Means	Simultaneous Upper Confidence Limit	•
0.062 - 0	-0.38058	-0.26667	-0.15276	***
0.124 - 0	-0.61391	-0.50000	-0.38609	***
0.25 - 0	-0.81391	-0.70000	-0.58609	***

oybean phytotoxicity

Transform: ARC SINE(SQUARE ROOT(Y)) ile: soy

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

ROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	1.000	1.345	1.345
2	0.001 lb ai/A	3	1.000	1.345	1.345
3	0.002 lb ai/A	3	1.000	1.345	1.345
4	0.004 lb ai/A	3	1.000	1.345	1.345
5	0.008 lb ai/A	3	0.933	1.281	1.281
6	0.015 lb ai/A	3	0.600	0.886	0.886
7	0.031 lb ai/A	3	0.367	0.650	0.650
8	0.062 lb ai/A	3	0.300	0.580	0.580
9	0.124 lb ai/A	3	0.200	0.464	0.464
10	0.25 lb ai/A	3 .	0.100	0.322	0.322

oybean phytotoxicity
ile: soy Trans Transform: ARC SINE(SQUARE ROOT(Y))

MITTTIAMS	TEST	(Isotonic	regression	model)	TABLE 2	OF	2
		TSOTONTZED	CALC	STG	ጥል ጽፒ ፑ		וח

IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Form. Con. 0.001 lb ai/A 0.002 lb ai/A 0.004 lb ai/A 0.008 lb ai/A 0.015 lb ai/A 0.031 lb ai/A 0.062 lb ai/A	1.345 1.345 1.345 1.345 1.281 0.886 0.650 0.580	0.000 0.000 0.000 3.013 21.568 32.670 35.960	* * *	1.72 1.81 1.83 1.85 1.86 1.86	k= 1, v=20 k= 2, v=20 k= 3, v=20 k= 4, v=20 k= 5, v=20 k= 6, v=20 k= 7, v=20
0.124 lb ai/A 0.25 lb ai/A	0.464 0.322	41.408 48.072	*	1.87 1.87	k= 8, v=20 k= 9, v=20

0.026

te: df used for table values are approximate when v > 20.

Nort - 6,008 16 ai/A

soybean phyto.

Estimated EC Values and Confidence Limits

		Lower	Upper
Point	Conc.	95% Confider	nce Limits
EC 1.00	0.0010	0.0000	0.0034
EC 5.00	0.0026	0.0002	0.0068
EC10.00	0.0045	0.0005	0.0101
EC15.00	0.0064	0.0011	0.0131
EC50.00	0.0295	0.0150	0.0505
EC85.00	0.1361	0.0737	0.5499
EC90.00	0.1954	0.0975	1.0658
EC95.00	0.3339	0.1450	2.8937
EC99.00	0.9121	0.2961	19.3822

Y= 1.56(x)+ 7.39.

F.C. : 0.011162/A

```
File:a:soy.out Page 1
                                                                                    |File:a:soy.out Page 2
                             soybean phytotoxicity
                                                                                                                  soybean phytotoxicity
                                                   15:35 Wednesday, May 21, 1997
                                                                                         MODEL: YOUNG = CO * PROBNOŔM ((LÒG_EC25 - LOG_CONC) / SIGMA - 0.67449)
                                                                                                                   WEIGHTED REGRESSION
       085
                CONC
                        LOG CONC
                                     Y 1
                                            Y2
                                                    Y3
                                                          Y4
                                                                Y5
                                                                      Y6
                                                                                                                                        15:35 Wednesday, May 21, 1997
              0.000
                                                                                                        Non-Linear Least Squares Iterative Phase
                        -2.09691
              0.008
                                    1.0
                                           0.9
                                                   0.9
                                                                                                    Dependent Variable COUNT Method: Gauss-Newton
              0.015
                        -1.82391
                                           0.6
                                    0.6
                                                  0.6
                                                                                                       LOG EC25
                                                                                           Iter
                                                                                                                         SIGMA
                                                                                                                                                  Weighted SS
              0.031
                        -1.50864
                                    0.3
                                           0.4
                                                  0.4
                                                                                                      -1.982000
                                                                                                                                      1.000000
                                                                                                                      0.641000
                                                                                                                                                     Ŏ.241390
              0.062
                        -1.20761
                                    0.3
                                           0.3
                                                  0.3
                                                                                                      -2.146243
                                                                                                                      0.761365
                                                                                                                                      1.061892
                                                                                                                                                     0.205596
              0.124
                        -0.90658
                                    0.2
                                           0.2
                                                  0.2
                                                                                                      -2.110110
                                                                                                                      0.740121
                                                                                                                                      1.044048
                                                                                                                                                     0.203876
              0.250
                        -0.60206
                                    0.1
                                           0.1
                                                   0.1
                                                                                                      -2.118154
                                                                                                                      0.744792
                                                                                                                                      1.047052
                                                                                                                                                     0.204142
                             soybean phytotoxicity
                                                                              32
                                                                                                     -2.116377
                                                                                                                      0.743753
                                                                                                                                      1.046374
                                                                                                                                                     0.204073
         MODEL: COUNT = CO * PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
                                                                                              5
                                                                                                      -2.116773
                                                                                                                      0.743984
                                                                                                                                      1.046523
                                                                                                                                                     0.204088
                              WEIGHTED REGRESSION
                                                                                                     -2.116685
                                                                                                                      0.743932
                                                                                                                                                     0.204085
                                                                                                                                      1.046490
                                                   15:35 Wednesday, May 21, 1997
                                                                                                      -2.116704
                                                                                                                      0.743944
                                                                                                                                      1.046497
                                                                                                                                                     0.204086
                                                                                                      -2.116700
                                                                                                                      0.743941
                                                                                                                                      1.046496
                                                                                                                                                     0.204086
                    Non-Linear Least Squares Iterative Phase
                                                                                                                      0.743942
                                                                                                                                      1.046496
                                                                                                      -2.116701
                                                                                                                                                     0.204086
               Dependent Variable COUNT Method: Gauss-Newton
                                                                                                                      0.743942
                                                                                                      -2.116701
                                                                                                                                      1.046496
                                                                                                                                                     0.204086
                 LOG EC50
      lter
                                    SIGMA
                                                             Weighted SS
                                                                                             11
                                                                                                      -2.116701
                                                                                                                      0.743942
                                                                                                                                      1.046496
                                                                                                                                                     0.204086
                 -1.530000
                                 0.641000
                                                1.000000
                                                                0.241481
                                                                                     NOTE: Convergence criterion met.
                 -1.632722
                                 0.761343
                                                1.061890
                                                                0.205595
                 -1.610909
                                 0.740124
                                                1.044049
                                                                0.203876
                 -1.615798
                                 0.744791
                                                1.047051
                                                                0.204142
                                                                                        Non-Linear Least Squares Summary Statistics
                                                                                                                                         Dependent Variable COUNT
                 -1.614723
                                 0.743753
                                                1.046374
                                                                0.204074
                -1.614963
                                 0.743984
                                                1.046523
                                                                0.204088
                                                                                            Source
                                                                                                                         Weighted SS
                                                                                                                                          Weighted MS
                 -1.614910
                                 0.743932
                                                1.046490
                                                                0.204085
                 -1.614922
                                 0.743944
                                                1.046497
                                                                0.204086
                                                                                            Regression
                                                                                                                        10.500000000
                                                                                                                                          3.500000000
         8
                 -1.614919
                                 0.743941
                                                1.046496
                                                                0.204086
                                                                                            Residual
                                                                                                                   18
                                                                                                                         0.204085645
                                                                                                                                          0.011338091
                 -1.614920
                                 0.743942
                                                1.046496
                                                                0.204086
                                                                                                                        10.704085645
                                                                                            Uncorrected Total
                                                                                                                   21
        10
                 -1.614919
                                 0.743942
                                                1.046496
                                                                0.204086
        11
                 -1.614920
                                 0.743942
                                                1.046496
                                                                0.204086
                                                                                                                   20
                                                                                                                         4.869140224
                                                                                            (Corrected Total)
NOTE: Convergence criterion met.
                                                                                            Parameter
                                                                                                          Estimate
                                                                                                                       Asymptotic
                                                                                                                                               Asymptotic 95 %
   Non-Linear Least Squares Summary Statistics
                                                    Dependent Variable COUNT
                                                                                                                                           Confidence Interval
                                                                                                                       Std. Error
                                                                                                                                           Lower
       Source
                                    Weighted SS
                                                     Weighted MS
                                                                                            LOG EC25
                                                                                                      -2.116700769 0.10944486911 -2.3466343876
                                                                                                                                                 -1.8867671508
                                                                                               51GMA
                                                                                                       0.743941732 0.06387368708 0.6097489821 0.8781344827
       Regression
                                   10.500000000
                                                    3.500000000
                                                                                                       1.046495977 0.06138535919 0.9175309751 1.1754609789
       Residual
                                    0.204085645
                                                     0.011338091
       Uncorrected Total
                                   10.704085645
                                                                                                              Asymptotic Correlation Matrix
       (Corrected Total)
                                    4.869140224
                                                                                             Corr
                                                                                                                LOG EC25
                                                                                                                                      SIGMA
                                                                                                                                                           CO
                     Estimate
       Parameter
                                  Asymptotic
                                                          Asymptotic 95 %
                                                                                             LOG EC25
                                                                                                                               -0.885287687
                                                                                                                                                 -0.758497923
                                  Std. Error
                                                      Confidence Interval
                                                                                                SIGMA
                                                                                                            -0.885287687
                                                                                                                                                 0.5166567695
                                                                                                            -0.758497923
                                                                                                   CO
                                                                                                                              0.5166567695
       LOG EC50 -1.614919510 0.07406600954 -1.7705253938 -1.4593136264
                                                                                                                  soybean phytotoxicity
                  0.743941732 0.06387368708 0.6097489821 0.8781344827
          SIGMA
                                                                                         MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
             C0
                  1.046495977 0.06138535919 0.9175309751 1.1754609789
                                                                                                            SUMMARY OF NONLTHEAR REGRESSION
                                                                                                                                        15:35 Wednesday, May 21, 1997
                        Asymptotic Correlation Matrix
                                                                                         OBS
                                                                                                CONC
                                                                                                        LOG EC25
                                                                                                                      SIGMA
                                                                                                                                    CO.
                                                                                                                                            RESID SS
                                                                                                                                                           EC25
        Corr
                          LOG_EC50
                                                SIGMA
                                                                      CO
                                                                                          1
                                                                                                  0
                                                                                                         -2.11670
                                                                                                                     0.74394
                                                                                                                                1.04650
                                                                                                                                             0.20409
                                                                                                                                                         .0076436
                                                                                                                  soybean phytotoxicity
                                                                                                                                                                    36
        LOG EC50
                                         -0.726487524
                                                            -0.820282003
                                                                                         MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
           SIGMA
                       -0.726487524
                                                            0.5166567695
                                                                                                                                        T5:35 Wednesday, May 21, 1997
              CO.
                       -0.820282003
                                         0.5166567695
         soybean phytotoxicity
MODEL: COUNT = CO * PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
                                                                              33
                                                                                                      Plot of COUNT*LOG CONC. Symbol used is '0'.
                                                                                                      Plot of PRED*LOG CONC.
                                                                                                                                Symbol used is '.'.
                       SUMMARY OF NONLINEAR REGRESSION
                                                   15:35 Wednesday, May 21, 1997
                                                                                     COUNT
    OBS
           CONC
                   LOG EC50
                                 SIGMA
                                              CO
                                                       RESID_SS
                                                                     EC50
                                                                                       1.2
```

0

-1.61492

0.74394

1.04650

0.20409

0.024271

```
|File:a:soy.out Page 3
                                                                                    |File:a:soy.out Page 4
                                                                                    Source
                                                                                                                         Squares
                                                                                                                                         Square
                                                                                                                                                  F Value
                                                                                                                     2.26666667
                                                                                                                                     0.37777778
                                                                                                                                                   396.67
                                                                                    Model
                                                                                                              6
  1.0
             0
                                                                                                             14
                                                                                                                     0.01333333
                                                                                                                                     0.00095238
                                                                                    Error
             Ω
                                                                                                             20
                                                                                                                     2.28000000
                                                                                    Corrected Total
                                                                                                                           C.V.
                                                                                                                                       Root MSE
                                                                                                       R-Square
  0.8
                                                                                                       0.994152
                                                                                                                       6.172134
                                                                                                                                       0.030861
             . . .
                                                                                                                      Type I SS
                                                                                                                                    Mean Square
                                                                                                                                                 F Value
                                                                                    Source
                       Ò ...
  0.6
                                                                                    DOSE
                                                                                                              6
                                                                                                                     2.26666667
                                                                                                                                     0.37777778
                                                                                                                                                   396.67
                                                                                                             DF
                                                                                                                    Type III SS
                                                                                                                                    Mean Square
                                                                                                                                                  F Value
                                                                                    Source
                                                                                    DOSE
                                                                                                              6
                                                                                                                     2.26666667
                                                                                                                                     0.37777778
                                                                                                                                                   396.67
  0.4
                                                                                                       SOYDERN PHYTOTOXICITY COMPARISON OF MEANS FOR NOEL DETERMINATION
                                                .0..
                                                                                                         TEST IF TREATMENT IS LESS THAN CONTROL
                                                                                                                                       15:35 Wednesday, May 21, 1997
  0.2
                                                          ....0
                                                                                                            General Linear Models Procedure
                                                                                                                      ------RESPONSE------
                                                                                                      Level of
                                                                                                      DOSE
                                                                                                                         Mean
                                                                                                                                            SD
  0.0
                                                                                                                        1.00000000
                                                                                                                                         0.00000000
                                                                                                      0.25
                                                                                                                       0.10000000
                                                                                                                                         0.00000000
                                                                                                      0.008
                                                                                                                       0.93333333
                                                                                                                                         0.05773503
     -2.25
                -2.00
                          -1.75
                                    -1.50
                                              -1.25
                                                                                                      0.015
                                                                                                                        0.60000000
                                                                                                                                         0.00000000
                                                         -1.00
                                                                   -0.75
                                                                           -0.50
                                                                                                      0.031
                                                                                                                       0.36666667
                                                                                                                                         0.05773503
                                                                                                      0.062
                                                                                                                        0.30000000
                                                                                                                                         0.00000000
                                       LOG CONC
                                                                                                      0.124
                                                                                                                        0.2000000
                                                                                                                                         0.00000000
NOTE: 1526 obs had missing values. 1464 obs hidden.
                                                                                                                 soybean phytotoxicity
                             soybean phytotoxicity
                                                                              37
                                                                                                       COMPARISON OF MEAN'S FOR NOEL DÉTERMINATION
                  COMPARISON OF MEAN'S FOR NOEL DETERMINATION
                                                                                                         TEST IF TREATMENT IS LESS THAN CONTROL
                    TEST IF TREATMENT IS LESS THAN CONTROL
                                                                                                                                       15:35 Wednesday, May 21, 1997
                                                  15:35 Wednesday, May 21, 1997
                                                                                                            General Linear Models Procedure
                        General Linear Models Procedure
                                                                                                  Dunnett's One-tailed T tests for variable: RESPONSE
                            Class Level Information
                                                                                              NOTE: This tests controls the type I experimentwise error for
           Class
                    Levels
                               Values
                                                                                                    comparisons of all treatments against a control.
                               0 0.25 0.008 0.015 0.031 0.062 0.124
           DOSE
                                                                                                  Alpha= 0.05 Confidence= 0.95 df= 14 MSE= 0.000952
                                                                                                          Critical Value of Dunnett's T= 2.532
                                                                                                         Minimum Significant Difference= 0.0638
                   Number of observations in data set = 42
                                                                                           Comparisons significant at the 0.05 level are indicated by '***'.
NOTE: Due to missing values, only 21 observations can be used in this
      analysis.
                                                                                                                 Simultaneous
                                                                                                                                          Simultaneous
                                                                                                                                              Upper
                                                                                                                              Difference
                                                                                                                     Lower
                             soybean phytotoxicity
                                                                              38
                                                                                                     DOSE
                                                                                                                                           Confidence
                                                                                                                  Confidence
                                                                                                                                 Between
                  COMPARISON OF MEANS FOR NOEL DETERMINATION
                                                                                                  Comparison
                                                                                                                     Limit
                                                                                                                                 Means
                                                                                                                                              Limit
                    TEST IF TREATMENT IS LESS THAN CONTROL
                                                  15:35 Wednesday, May 21, 1997
                                                                                                0.008 - 0
                                                                                                                   -0.13047
                                                                                                                               -0.06667
                                                                                                                                            -0.00286
                                                                                                0.015 - 0
                                                                                                                   -0.46381
                                                                                                                               -0.40000
                                                                                                                                           -0.33619
                                                                                                0.031 - 0
                                                                                                                   -0.69714
                                                                                                                               -0.63333
                                                                                                                                           -0.56953
                        General Linear Models Procedure
                                                                                                                               -0.70000
                                                                                                0.062 - 0
                                                                                                                   -0.76381
                                                                                                                                           -0.63619
Dependent Variable: RESPONSE
                                                                                                0.124 - 0
                                                                                                                   -0.86381
                                                                                                                               -0.80000
                                                                                                                                           -0.73619
                                                                                                                   -0.96381
                                                                                                                               -0.90000
                                                                                                                                           -0.83619
                                     Sum of
                                                      Mean
```

Pr > F

0.0001

**RESPONSE Mean** 

0.500000

Pr > F

0.0001

Pr > F

0.0001

39

40

\*\*\*

\*\*\* \*\*\*

sunflower phytotoxicity

File: sun Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

ROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	1.000	1.345	1.345
2	0.001 lb ai/A	3	1.000	1.345	1.345
3	0.002 lb ai/A	3	0.867	1.202	1.202
4	0.004 lb ai/A	3	0.767	1.077	1.077
5	0.008 lb ai/A	3	0.300	0.580	0.580
6	0.015 lb ai/A	3	0.267	0.541	0.541
7	0.031 lb ai/A	3	0.100	0.322	0.322
8	0.062 lb ai/A	3	0.100	0.322	0.322
9	0.124 lb ai/A	3	0.033	0.258	0.258
10	0.25 lb ai/A	3	0.000	0.226	0.226

unflower phytotoxicity

ile: sun Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 2 OF 2

IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Form. Con.	1.345				
0.001 lb ai/A	1.345	0.000		1.72	k = 1, v = 20
0.002 lb ai/A	1.202	2.910	*	1.81	k = 2, v = 20
0.004 lb ai/A	1.077	5.436	*	1.83	k = 3, v = 20
0.008 lb ai/A	0.580	15.521	*	1.85	k = 4, v = 20
0.015 lb ai/A	0.541	16.305	*	1.86	k = 5, v = 20
0.031 lb ai/A	0.322	20.749	*	1.86	k = 6, v = 20
0.062 lb ai/A	0.322	20.749	*	1.86	k = 7, v = 20
0.124 lb ai/A	0.258	22.050	*	1.87	k = 8, v = 20
0.25 lb ai/A	0.226	22.700	*	1.87	k = 9, v = 20

= 0.060

pte: df used for table values are approximate when v > 20.

NOCE - O. not 16 JA

sunflower phyto.

#### Estimated EC Values and Confidence Limits

		Lower	Upper
Point	Conc.	95% Confider	nce Limits
EC 1.00	0.0006	0.0004	0.0009
EC 5.00	0.0013	0.0009	0.0017
EC10.00	0.0019	0.0014	0.0024
EC15.00	0.0025	0.0019	0.0030
EC50.00	0.0074	0.0063	0.0086
EC85.00	0.0221	0.0178	0.0292
EC90.00	0.0287	0.0225	0.0395
EC95.00	0.0422	0.0316	0.0621
EC99.00	0.0868	0.0594	0.1457

y= 2.17(x)+ 9.63

EC = 0.00+11 = 1A

7 2001

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|File:a:sun.out Page 1
                                                                                     |File:a:sun.out Page 2
                            sunflower phytotoxicity
                                                                                            Iter
                                                                                                       LOG EC25
                                                                                                                           SIGMA
                                                                                                                                             CO
                                                                                                                                                    Weighted SS
                                                    15:35 Wednesday, May 21, 1997
                                                                                                       -2.398000
                                                                                                                       0.461000
                                                                                                                                       1.000000
                                                                                                                                                       Ď. 102974
                                                                                                       -2.460121
                                                                                                                       0.471489
                                                                                                                                       1.006580
                                                                                                                                                       0.081679
       085
                CONC
                        LOG CONC
                                     Y1
                                             Y2
                                                     Y3
                                                            Y4
                                                                  Y5
                                                                        Y6
                                                                                                       -2.455473
                                                                                                                       0.466996
                                                                                                                                       1.005398
                                                                                                                                                       0.081496
                                                                                                       -2.455900
                                                                                                                       0.467239
                                                                                                                                       1.005600
1.005586
                                                                                                                                                       0.081507
               0.000
                                     1.0
                                            1.00
                                                    1.0
                                                                                                       -2.455870
                                                                                                                       0.467222
                                                                                                                                                       0.081506
                        -2.69897
        3
               0.002
                                            0.90
                                    0.8
                                                    0.9
                                                                                               5
                                                                                                       -2.455872
                                                                                                                       0.467223
                                                                                                                                       1.005587
                                                                                                                                                       0.081506
              0.004
                        -2.39794
                                    0.7
                                            0.70
                                                    0.9
                                                                                                                       0.467223
                                                                                                       -2.455872
                                                                                                                                       1.005587
                                                                                                                                                       0.081506
              0.012
                        -1.92082
                                                    0.3
                                    0.3
                                            0.25
                                                                                                                                       1.005587
                                                                                                       -2.455872
                                                                                                                       0.467223
                                                                                                                                                       0.081506
              0.031
                        -1.50864
                                    0.1
                                            0.10
                                                    0.1
                                                                                      NOTE: Convergence criterion met.
         sunflower phytotoxicity

MODEL: COUNT = CO * PROBNORM ((LOG ECSO - LOG CONC) / SIGMA)
                                                                               42
                              WEIGHTED REGRESSION
                                                                                         Non-Linear Least Squares Summary Statistics
                                                                                                                                           Dependent Variable COUNT
                                                   15:35 Wednesday, May 21, 1997
                                                                                             Source
                                                                                                                           Weighted SS
                                                                                                                                            Weighted MS
               Non-Linear Least Squares Iterative Phase
Dependent Variable COUNT Method: Gauss-Newton
                                                                                             Regression
                                                                                                                          9.0500000000
                                                                                                                                          3.0166666667
      Iter
                 LOG EC50
                                    SIGMA
                                                       CO
                                                             Weighted SS
                                                                                             Residual
                                                                                                                    12
                                                                                                                          0.0815064578
                                                                                                                                          0.0067922048
                 -2.131000
                                 0.461000
                                                 1.000000
                                                                 0.081269
                                                                                             Uncorrected Total
                                                                                                                    15
                                                                                                                         9.1315064578
                 -2.141255
                                 0.467764
                                                 1.005980
                                                                 0.081531
                 -2.140695
                                 0.467187
                                                 1.005556
                                                                 0.081505
                                                                                             (Corrected Total)
                                                                                                                          4.8525894014
                 -2.140738
                                 0.467226
                                                 1.005589
                                                                 0.081507
                 -2.140735
                                 0.467223
                                                 1.005587
                                                                 0.081506
                 -2.140735
                                 0.467223
                                                 1.005587
                                                                 0.081506
                                                                                             Parameter
                                                                                                            Estimate
                                                                                                                         Asymptotic
                                                                                                                                                 Asymptotic 95 %
                 -2.140735
                                 0.467223
                                                 1.005587
                                                                 0.081506
                                                                                                                         Std. Error
                                                                                                                                             Confidence Interval
NOTE: Convergence criterion met.
                                                                                                                                             Lower
                                                                                             LOG EC25 -2.455872312 0.06526284057 -2.5980680358 -2.3136765883
                                                                                                        0.467223416 0.03772768729 0.3850217255 0.5494251059
                                                                                                SIGMA
   Non-Linear Least Squares Summary Statistics
                                                     Dependent Variable COUNT
                                                                                                        1.005587004 0.04404034942 0.9096311838 1.1015428232
       Source
                                    Weighted SS
                                                     Weighted MS
                                                                                                               Asymptotic Correlation Matrix
       Regression
                                   9.0500000000
                                                    3.0166666667
       Residual
                                   0.0815064577
                                                    0.0067922048
                                                                                              Corr
                                                                                                                 LOG_EC25
                                                                                                                                                             CO
                                                                                                                                       SIGMA
       Uncorrected Total
                              15
                                   9.1315064577
                                                                                              LOG EC25
                                                                                                                                -0.883906957
                                                                                                                                                   -0.755786531
       (Corrected Total)
                                   4.8525894041
                                                                                                 SIGMA
                                                                                                             -0.883906957
                                                                                                                                                   0.5774877679
                                                                                                    CO
                                                                                                             -0.755786531
                                                                                                                                0.5774877679
                                                                                          sunflower phytotoxicity
MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
       Parameter
                     Estimate
                                  Asymptotic
                                                          Asymptotic 95 %
                                  Std. Error
                                                      Confidence Interval
                                                                                                              SUMMARY OF NONLTHEAR REGRESSION
                                                      Lower
                                                                                                                                         15:35 Wednesday, May 21, 1997
       LOG EC50 -2.140734789 0.04439483769 -2.2374630824 -2.0440064957
          $1GMA
                  0.467223414 0.03772768723 0.3850217244 0.5494251045
                                                                                          OBS
                                                                                                 CONC
                                                                                                          LOG EC25
                                                                                                                       SIGMA
                                                                                                                                              RESID SS
                                                                                                                                                            EC25
                 1.005587002 0.04404034934 0.9096311830 1.1015428220
                                                                                                   0
                                                                                                          -2.45587
                                                                                                                      0.46722
                                                                                                                                             0.081506
                                                                                                                                 1.00559
                                                                                                                                                           .0035005
                                                                                                                  sunflower phytotoxicity
                         Asymptotic Correlation Matrix
                                                                                          MODEL: YOUNG = CO * PROBNORM ((LOG ÉC25 - LOG CONC) / SIGMA - 0.67449)
                                                                                                                                         T5:35 Wednesday, May 21, 1997
        Corr
                           LOG EC50
                                                 SIGMA
                                                                       C0
                                                                                                        Plot of COUNT*LOG CONC. Symbol used is '0'.
        LOG EC50
                                          -0.726194674
                                                             -0.780032939
                                                                                                        Plot of PRED*LOG CONC.
                                                                                                                                  Symbol used is '.'.
                       -0.726194674
           SIGMA
                                                            0.5774877683
                       -0.780032939
              C0
                                         0.5774877683
                                                                                      COUNT
                            sunflower phytotaxicity
                                                                               43
         MODEL: COUNT = CO * PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
                                                                                        1.0
                        SUMMARY OF NONLINEAR REGRESSION
                                                   15:35 Wednesday, May 21, 1997
                                                                                                 0.
                                                                                                                 0
    OBS
           CONC
                   LOG EC50
                                 SIGMA
                                                       RESID SS
                                                                      EC50
             0
                    -2.14073
                                0.46722
                                          1.00559
                                                       0.081506
                                                                    .0072321
                                                                                        0.8
                                                                                                 0
                            sunflower phytotoxicity
    MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
                              WEIGHTED REGRESSION
                                                                                                                 0..
                                                   15:35 Wednesday, May 21, 1997
                   Non-Linear Least Squares Iterative Phase
                                                                                        0.6
               Dependent Variable COUNT Method: Gauss-Newton
```

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		•••			
0.4		•••	•		
0.4			•••		
			···.		
1			0		
0.2		·	•	•••	
				•••••	0
				••	
0.0					
-2.8	-2.6 -2.4	-2.2	-2.0 -1.	8 -1.6	-1.4
		roe_co	HC .		
NOTE: 1215 obs	had missing v	alues. 1140 obs	hidden.		
	COMPARISON	Inflower phytoto OF MEANS FOR NO	EL DETERMINATI		47
	TEST IF T	REATMENT IS LES	S THAN CONTROL 15:35 Wed	nesday, May	21, 1997
		al Linear Models			
	C	lass Level Infor	mation		
	Class Lev	vels Values			
1	DOSE	5 0 0.002	0.004 0.012 0.	031	
	Number of	observations in	data set = 30		
NOTE: Due to mi analysis.		only 15 observe	itions can be u	sed in this	
	SU	unflower phytoto	xicity		48
		OF MEANS FOR NO TREATMENT IS LES	S THAN CONTROL		21, 1997
	Genera	al Linear Models	Procedure		
Dependent Varia	ble: RESPONSE				
Source	DF	Sum of Squares	Mean Square	F Value	Pr⊳> F
Model	4	1.82733333	0.45683333	130.52	0.0001
Error	10	0.03500000	0.00350000		
Corrected Total	14	1.86233333			
	R-Square	C.V.	Root MSE	RESP	ONSE Mean
	0.981206	9.805657	0.059161		0.603333
Source \	DF	Type I SS	Mean Square	F Value	· Pr > F
DOSE 🧸 🥄	4	1.82733333	0.45683333	130.52	0.0001

File:a:sun.out Source	Page 4	DF	Type III SS	Mean Square	F Value	Pr > F
DOSE		4	1.82733333	0.45683333	130.52	0.0001

sunflower phytotoxicity 49
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL
15:35 Wednesday, May 21, 1997

#### General Linear Models Procedure

Level of		RESPO			
DOSE	N	Mean	SD		
0	3	1.00000000	0.00000000		
0.002	3	0.86666667	0.05773503		
0.004	3	0.76666667	0.11547005		
0.012	3	0.28333333	0.02886751		
0.031	3	0.10000000	0.0000000		
0.05.	sunf	lower phytotoxic			50
COMPARIS		MEANS FOR NOEL I			
		ATMENT IS LESS TO			
			15:35 Vednesday	. May 21.	1997

#### General Linear Models Procedure

Dunnett's One-tailed I tests for variable: RESPONSE

NOTE: This tests controls the type 1 experimentwise error for comparisons of all treatments against a control.

Alpha= 0.05 Confidence= 0.95 df= 10 MSE= 0.0035 Critical Value of Dunnett's T= 2.466 Minimum Significant Difference= 0.1191

Comparisons significant at the 0.05 level are indicated by '\*\*\*'.

DOSE Comparison	Simultaneous Lower Confidence Limit	Difference Between Means	Simultaneous Upper Confidence Limit	;
0.002 - 0	-0.25243	-0.13333	-0.01424	***
0.004 - 0	-0.35243	-0.23333	-0.11424	
0.012 - 0	-0.83576	-0.71667	-0.59757	
0.031 - 0	-1.01910	-0.90000	-0.78090	

omato phytotoxicity

ile: tom Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

ROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZĖD MEAN
1	Form. Con.	3	0.933	1.281	1.281
2	0.001 lb ai/A	3	0.900	1.249	1.249
3	0.002 lb ai/A	3	0.867	1.202	. , 1.202
4	0.004 lb ai/A	3	0.700	0.995	0.995
5	0.008 lb ai/A	3	0.500	0.785	0.785
6	0.015 lb ai/A	3	0.300	0.580	0.580
7	0.031 lb ai/A	3	0.133	0.369	0.369
8	0.062 lb ai/A	3	0.000	0.226	0.226
9	0.124 lb ai/A	3	0.000	0.226	0.226
10	0.25 lb ai/A	3	0.000	0.226	0.226

omato phytotoxicity ile: tom Tran Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2 OF 2
---------------	-----------	------------	--------	--------------

IDENTIFICATION	ISOTONIZED	CALC.	SIG	TABLE	DEGREES OF
	MEAN	WILLIAMS	P=.05	WILLIAMS	FREEDOM
Form. Con. 0.001 lb ai/A 0.002 lb ai/A 0.004 lb ai/A 0.008 lb ai/A 0.015 lb ai/A 0.031 lb ai/A 0.062 lb ai/A 0.124 lb ai/A 0.25 lb ai/A	1.281 1.249 1.202 0.995 0.785 0.580 0.369 0.226 0.226	0.733 1.815 6.546 11.333 16.037 20.851 24.133 24.133	* * * * * * *	1.72 1.81 1.83 1.85 1.86 1.86 1.86 1.87	k= 1, v=20 k= 2, v=20 k= 3, v=20 k= 4, v=20 k= 5, v=20 k= 6, v=20 k= 7, v=20 k= 8, v=20 k= 9, v=20

<sup>0.054</sup> 

NOTEL = 0,001 16 a./A

te: df used for table values are approximate when v > 20.

tomato phyto.

Estimated EC Values and Confidence Limits

		Lower	Upper
Point	Conc.	95% Confide	nce Limits
EC 1.00	0.0006	0.0004	0.0009
EC 5.00	0.0014	0.0009	0.0019
EC10.00	0.0022	0.0016	0.0028
EC15.00	0.0030	0.0022	0.0036
EC50.00	0.0104	0.0089	0.0122
EC85.00	0.0364	0.0283	0.0509
EC90.00	0.0490	0.0368	0.0723
EC95.00	0.0760	0.0539	0.1221
EC99.00	0.1736	0.1100	0.3279

Y= 1.80(x) + 8.77

ECz; = 0,005 16 21A

12/1/2/

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                                                                                     Ifile:a:tom.out Page 2
                              tomato phytotoxicity
                                                                                                         Non-Linear Least Squares Iterative Phase
                                                   15:35 Wednesday, May 21, 1997
                                                                                                     Dependent Variable COUNT Method: Gauss-Newton
                                                                                                       LOG EC25
                                                                                                                          SIGMA
                                                                                                                                                   Weighted SS
                                                                                            lter
       OBS:
               CONC
                       LOG CONC
                                     Y 1
                                            Y2
                                                    Y3
                                                          Y4
                                                                Y5
                                                                                                                                       0.930000
                                                                                                       -2.301000
                                                                                                                       0.526000
                                                                                                                                                      0.210796
                                                                                                      -2.412531
                                                                                                                       0.518715
                                                                                                                                       0.944711
                                                                                                                                                      0.096114
              0.000
                                    1 0
                                                                                                                       0.503957
                                                                                                                                       0.942737
                                                                                                      -2.396537
                                                                                                                                                      0.096474
                        -2.69897
              0.002
                                    0.8
                                           0.9
                                                   0.9
                                                                                                       -2.397853
                                                                                                                                       0.943248
                                                                                                                       0.504866
                                                                                                                                                      0.096411
              0.004
                        -2.39794
                                    0.6
                                           0.8
                                                   0.7
                                                                                                       -2.397782
                                                                                                                       0.504819
                                                                                                                                       0.943216
                                                                                                                                                      0.096414
              0.008
                        -2.09691
                                    0.5
                                           0.5
                                                   0.5
                                                                                                       -2.397786
                                                                                                                       0.504822
                                                                                                                                       0.943218
                                                                                                                                                      0.096414
              0.015
                        -1.82391
                                    0.3
                                           0.3
                                                   0.3
                                                                                                       -2.397786
                                                                                                                       0.504822
                                                                                                                                       0.943218
                                                                                                                                                       0.096414
              0.031
                        -1.50864
                                           0.1
                                    0.2
                                                   0.1
                                                                                                       -2.397786
                                                                                                                       0.504822
                                                                                                                                       0.943218
                                                                                                                                                      0.096414
        tomato phytotoxicity

MODEL: COUNT = CO:* PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
                                                                               52
                                                                                      NOTE: Convergence criterion met.
                              WEIGHTED REGRESSION
                                                   15:35 Wednesday, May 21, 1997
                                                                                         Non-Linear Least Squares Summary Statistics
                                                                                                                                           Dependent Variable COUNT
                   Non-Linear Least Squares Iterative Phase
                                                                                                                          Weighted SS
                                                                                             Source
                                                                                                                                           Weighted MS
               Dependent Variable COUNT Method: Gauss-Newton
                 LOG EC50
      Iter
                                    SIGMA
                                                       CO
                                                             Weighted SS
                                                                                                                          10.300000000
                                                                                             Regression
                                                                                                                                           3.433333333
                -1.983000
                                 0.526000
                                                 0.930000
                                                                0.146946
                                                                                             Residual
                                                                                                                          0.096414131
                                                                                                                                           0.006427609
                                                0.944132
                -2.060957
                                 0.511022
                                                                 0.096256
                                                                                             Uncorrected Total
                                                                                                                         10.396414131
                -2.056993
                                 0.504473
                                                 0.942997
                                                                 0.096435
                                 0.504840
                -2.057304
                                                 0.943230
                                                                 0.096413
                                                                                             (Corrected Total)
                                                                                                                    17
                                                                                                                          3.871044304
                -2.057288
                                 0.504821
                                                 0.943217
                                                                 0.096414
                 -2.057288
                                 0.504822
                                                 0.943218
                                                                0.096414
                                                 0.943218
                 -2.057288
                                 0.504822
                                                                0.096414
                                                                                             Parameter
                                                                                                            Estimate
                                                                                                                        Asymptotic
                                                                                                                                                Asymptotic 95 %
                -2.057288
                                 0.504822
                                                 0.943218
                                                                0.096414
                                                                                                                        Std. Error
                                                                                                                                            Confidence Interval
NOTE: Convergence criterion met.
                                                                                                                                            Lower
                                                                                             LOG EC25 -2.397785724 0.06615161849 -2.5387840248 -2.2567874225
SIGMA 0.504821848 0.04276711005 0.4136662570 0.5959774385
   Non-Linear Least Squares Summary Statistics
                                                     Dependent Variable COUNT
                                                                                                        0.943217755 0.04078024503 0.8562970508 1.0301384594
       Source
                                    Weighted SS
                                                     Weighted MS
                                                                                                               Asymptotic Correlation Matrix
       Regression
                                   10.300000000
                                                     3.433333333
       Residual
                              15
                                    0.096414131
                                                     0.006427609
                                                                                              Corr
                                                                                                                 LOG EC25
                                                                                                                                       SIGMA
                                                                                                                                                             CO
       Uncorrected Total
                              18
                                   10.396414131
                                                                                              LOG EC25
                                                                                                                                -0.887577795
                                                                                                                                                   -0.783099514
       (Corrected Total)
                              17
                                    3.871044305
                                                                                                             -0.887577795
                                                                                                 SIGMA
                                                                                                                                                   0.5890938067
                                                                                                             -0.783099514
                                                                                                                               0.5890938067
                                                                                                    CO
                                                                                                                    tomato phytotoxicity
       Parameter
                     Estimate
                                  Asymptotic
                                                          Asymptotic 95 %
                                                                                          MODEL: YOUNG = CO * PROBNORM ((LOG EC25 - LOG CONC) / SIGMA - 0.67449)
                                  Std. Error
                                                      Confidence Interval
                                                                                                             SUMMARY OF NONLTHEAR REGRESSION
                                                                                                                                         15:35 Wednesday, May 21, 1997
       LOG_EC50 -2.057288435 0.04267036610 -2.1482378221 -1.9663390487
                  0.504821848 0.04276711004 0.4136662568 0.5959774383
          SIGMA
                                                                                          OBS
                                                                                                 CONC
                                                                                                         LOG EC25
                                                                                                                                             RESID_SS
                                                                                                                                                            EC25
                  0.943217755 0.04078024502 0.8562970507 1.0301384592
                                                                                                   0
                                                                                                          -2.39779
                                                                                                                      0.50482
                                                                                                                                 0.94322
                                                                                                                                             0.096414
                                                                                                                                                           .0040014
                                                                                                                    tomato phytotoxicity
                        Asymptotic Correlation Matrix
                                                                                          MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
                                                                                                                                         T5:35 Wednesday, May 21, 1997
        Corr
                          LOG EC50
                                                 SIGMA
                                                                       CO
                                                                                                       Plot of COUNT*LOG CONC. Symbol used is '0'.
        LOG EC50
                                          -0.699987423
                                                             -0.815795845
                                                                                                       Plot of PRED*LOG CONC. Symbol used is '.'.
           SIGMA
                       -0.699987423
                                                            0.5890938067
                       -0.815795845
                                         0.5890938067
                                                                                      COUNT
                              tomato phytotoxicity
                                                                               53
        MODEL: COUNT = CO * PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
                                                                                        1.0
                       SUMMARY OF NONLINEAR REGRESSION
                                                   15:35 Wednesday, May 21, 1997
                                                                                                 0
   OBS
           CONC
                   LOG EC50
                                 SIGMA
                                               CO
                                                       RESID_SS
                                                                      EC50
             0
                   -2.05729
                                0.50482
                                           0.94322
                                                       0.096414
                                                                    .0087642
                                                                                        0.8
                              tomato phytotoxicity
   MODEL: YOUNG = CO * PROBNORM ((LOG EC25 - LOG CONC) / SIGMA - 0.67449)
                              WEIGHTED REGRESSION
                                                                                                                .0..
                                                   15:35 Wednesday, May 21, 1997
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File:a:tom.out 8	Page 3				
0.0		••••			
		···.			•
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0.4			•••		
			• • •		
			• •	• •	
0.2				••••	0
			•	••••	
•					0
0.0					
-2.8 -2	2.6 -2.4	-2.2	-2.0 -1.8	-1.6	-1.4
		roc_co	NC		
IOTE: 1218 obs ha					
		omato phytotox OF MEANS FOR NO	icity El determinatio	אכ	57
		EATMENT IS LES	S THAN CONTROL		24 4007
			15:35 Wedi	nesday, May	21, 1997
		. Linear Models ass Level Infor			
Cla	ss Levels	Values			
DOS	E 6	0 0.002 0.0	04 0.008 0.015	0.031	
	Number of o	observations in	data set = 36		
IOTE: Due to miss analysis.	ing values, o	only 18 observa	tions can be u	sed in this	
·	t	omato phytotox	icity		58
	COMPARISON C	OF MEANS FOR NO	EL DÉTERMINATIO	ON	
	IESI IF IN	CEATMENT 15 LFS	S THAN CONTROL 15:35 Wed	nesday, May	21, 1997
	General	Linear Models	Procedure		
ependent Variabl	e: RESPONSE				
ource	DF	Sum of Squares	Mean Square	f Value	Pr > F
odel	5	1.51611111	0.30322222	90.97	0.0001
rror	12	0.04000000	0.00333333	70.71	0.0001
Corrected Total	17	1.55611111	0.00000		
orrected rotat	R-Square	C.V.	Root MSE	PE CD	ONSE Mean
				RESPI	
•	0.974295	10.08962	0.057735		0.572222
Source .	DF	Type I SS	Mean Square	F Value	Pr > F

File:a:tom.out DOSE	Page 4	5	1.51611111	0.30322222	90.97	0.0001
Source		DF	Type III \$\$	Mean Square	F Value	Pr > F
DOSE		5	1.51611111	0.30322222	90.97	0.0001

tomato phytotoxicity

COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL
15:35 Wednesday, May 21, 1997

#### General Linear Models Procedure

Level of		RESPO	NSE	
DOSE	N	Mean	SD	
0	3	0.93333333	0.05773503	
0.002	3	0.86666667	0.05773503	
0.004	3	0.7000000	0.10000000	
0.008	3	0.50000000	0.0000000	
0.015	3	0.3000000	0.0000000	
0.031	3	0.13333333	0.05773503	
	tor	mato phytotoxicii	ty	60
COMPARIS	ON OF	MEAN'S FOR NOEL (	DÉTERMINATION	
TEST I	F TREA	ATMENT IS LESS TH	IAN CONTROL	

TEST IF TREATMENT IS LESS THAN CONTROL
15:35 Wednesday, May 21, 1997

General Linear Models Procedure

Dunnett's One-tailed T tests for variable: RESPONSE

NOTE: This tests controls the type I experimentwise error for comparisons of all treatments against a control.

Alpha= 0.05 Confidence= 0.95 df= 12 MSE= 0.003333 Critical Value of Dunnett's T= 2.502 Minimum Significant Difference= 0.118

Comparisons significant at the 0.05 level are indicated by '\*\*\*'.

DOSE Comparison	Simultaneous Lower Confidence Limit	Difference Between Means	Simultaneous Upper Confidence Limit	•
0.002 - 0	-0.18462	-0.06667	0.05129	***
0.004 - 0	-0.35129	-0.23333	-0.11538	
0.008 - 0	-0.55129	-0.43333	-0.31538	
0.015 - 0	-0.75129	-0.63333	-0.51538	
0.031 - 0	-0.91795	-0.80000	-0.68205	

orn phytotoxicity

'ile: cor Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 1 0	OF	7
-----------------------------------------------------	----	---

ROUP	IDENTIFICATION	N 	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	1.000	1.345	1.345
2	0.015 lb ai/A	3	1.000	1.345	1.345
3	0.031 lb ai/A	3	0.967	1.313	1.313
4	0.062 lb ai/A	3	0.867	1.202	1.202
5	0.124 lb ai/A	3	0.800	1.116	1.116
6	0.25 lb ai/A	3	0.700	0.995	0.995

orn phytotoxicity

ile: cor Transform: ARC SINE(SQUARE ROOT(Y))

	(Isotonic	=		TABLE 2	
	ISOTONIZED		SIG	TABLE	DEGREES

IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Form. Con.	1.345				
0.015 lb ai/A	1.345	0.000		1.78	k = 1, v = 12
0.031 lb ai/A	1.313	0.489		1.87	k=2, v=12
0.062 lb ai/A	1.202	2.189	*	1.90	k = 3, v = 12
0.124 lb ai/A	1.116	3.500	*	1.92	k = 4, v = 12
0.25 lb ai/A	0.995	5.345	*	1.93	k= 5, v=12

= 0.080

ote: df used for table values are approximate when v > 20.

NOTE - 6 051 16 ailA

# corn phyto.

Estimated EC Values and Confidence Limits

		Lower	Upper
Point	Conc.	95% Confidence	ce Limits
EC 1.00	0.0095	0.0021	0.0194
EC 5.00	0.0318	0.0139	0.0483
EC10.00	0.0603	0.0365	0.0813
EC15.00	0.0930	0.0663	0.1221
EC50.00	0.5796	0.3521	1.6069
EC85.00	3.6127	1.3771	28.7012
EC90.00	5.5698	1.8939	56.9931
EC95.00	10.5781	3.0337	157.6531
EC99.00	35.2276	7.3250	1065.1189

Y= 5.31 + 1.30(x) =C25 = 0.176 // wild nion phytotoxicity

ile: oni Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

ROUP	IDENTIFICATION	N 	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	1.000	1.345	1.345
2	0.015 lb ai/A	3	1.000	1.345	1.345
3	0.031 lb ai/A	3	1.000	1.345	1.345
4	0.062 lb ai/A	3	0.867	1.195	1.195
5	0.124 lb ai/A	3	0.767	1.068	1.073
6	0.25 lb ai/A	3	0.767	1.077	1.073

nion phytotoxicity

ile: oni Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 2 OF 2

IDENTIFICATION	ISOTONIZED	CALC.	SIG	TABLE	DEGREES OF
	MEAN	WILLIAMS	P=.05	WILLIAMS	FREEDOM
Form. Con. 0.015 lb ai/A 0.031 lb ai/A 0.062 lb ai/A 0.124 lb ai/A 0.25 lb ai/A	1.345 1.345 1.345 1.195 1.073	0.000 0.000 1.836 3.332 3.332	*	1.78 1.87 1.90 1.92 1.93	k= 1, v=12 k= 2, v=12 k= 3, v=12 k= 4, v=12 k= 5, v=12

= 0.100

NICEL : CICCE 16 a-14

te: df used for table values are approximate when v > 20.

wheat phytotoxicity

File: whe Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Form. Con.	3	0.867	1.202	1.202
2 3	0.015 lb ai/A 0.031 lb ai/A	3 3	0.867 0.833	1.202 1.154	1.202 1.154
4	0.062 lb ai/A	3	0.833	1.154	1.154
5 6	0.124 lb ai/A 0.25 lb ai/A	3 3	0.733 0.633	1.030 0.921	1.030 0.921

wheat phytotoxicity File: whe Tra Transform: ARC SINE(SQUARE ROOT(Y))

WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2 OF 2
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IDENTIFICATION	ISOTONIZED	CALC.	SIG	TABLE	DEGREES OF
	MEAN	WILLIAMS	P=.05	WILLIAMS	FREEDOM
Form. Con. 0.015 lb ai/A 0.031 lb ai/A 0.062 lb ai/A 0.124 lb ai/A 0.25 lb ai/A	1.202 1.202 1.154 1.154 1.030 0.921	0.000 0.758 0.758 2.755 4.498	* *	1.78 1.87 1.90 1.92 1.93	k= 1, v=12 k= 2, v=12 k= 3, v=12 k= 4, v=12 k= 5, v=12

0.076

Note: df used for table values are approximate when v > 20.

NOLL C. C.C. 16 wife

# DATA EVALUATION RECORD AQUATIC INVERTEBRATE LIFE CYCLE TEST GUIDELINE 72-4(B)

1. CHEMICAL: Fluroxypyr MHE PC Code No.: 128968

2. TEST MATERIAL: Fluroxypyr 1-Methylheptyl Purity: 95.8%

Ester

3. CITATION:

Authors: H.D. Kirk, J.A. Miller, J.M. Hugo and

A.M. Landre

<u>Title</u>: Evaluation of the Chronic Toxicity of

Fluroxypyr 1-Methylheptyl Ester to the

Daphnid, Daphnia magna Straus

Study Completion Date: July 15, 1996

Laboratory: The Toxicology Research Laboratory, The

Dow Chemical Company, Midland, MI

Sponsor: DowElanco, Indianapolis, IN

<u>Laboratory Report ID</u>: DECO-ES-3079

MRID No.: 440803-14

<u>DP Barcode</u>: D231718 and D236845

4. REVIEWED BY: Renee Costello, Biologist

Signature: Romée Costello Date: 7/24/97

APPROVED BY: Andy Bryceland, Aquatic Biologist

6. STUDY PARAMETERS:

5.

Age of Test Organism: <24 hours
Definitive Test Duration: 21 days

Study Method: Flow-Through
Type of Concentrations: Mean Measured

7. CONCLUSIONS: This study is scientifically sound but does not fulfill the guideline requirements for a freshwater invertebrate life-cycle test using Daphnia magna. Testing was conducted at above the solubility limit. It is likely that there was some undissolved test material in the system, this was not reported. Also, by placing the samples in acetonitrile, any suspended particles would have dissolved and the actual test concentrations to which the organisms were exposed is unknown. It is likely that the reported measured concentrations are an overestimate.

#### Results Synopsis:

NOEC: 60.5 ppb LOEC: 109 ppb MATC: 81.2 ppb

LOEC's for specific effects: Neonates Produced: 109 ppb Daphnid Survival: 499 ppb Growth (length): 174 ppb

#### 8. ADEQUACY OF THE STUDY:

- A. Classification: Supplemental
- B. Rationale: Undissolved particulates not reported. No filtration or centrifugation of test material. The measured concentration do not represent actual exposures.
- C. Repairability: May be upgraded with submission of particulate matter observations. Also, reporting if filtration was used in the test.
- 9. <u>GUIDELINE DEVIATIONS</u>: Since there is no SEP for a flow-through daphnid life-cycle test, the SEP for static renewal tests was used as general guidance in this data review.
  - 1. Dry weights of surviving adult daphnids were not measured as recommended in the guidelines.
  - 2. In this study, four replicates each containing 5 daphnids were used for each treatment level. The guidelines recommend that 7 test chambers with 1 daphnid each and 3 test chambers with 5 daphnids each be used.
  - 3. The concentration of solvent (acetone) was not the same in all treatment concentrations. The amount of solvent (acetone) in the solvent control was equivalent to the amount present in the highest test concentration.
  - 4. The dilution water was "softer"  $(67 76 \text{ mg/l as } CaCO_3)$  than what the guidelines recommend  $(160 \text{ to } 180 \text{ mg/l as } CaCO_3)$ .
  - 5. The authors did not report any undissolved test material. This was expected as the test was conducted at above the solubility limit of the material.
  - 6. The authors did not report if filtration or centrifugation of the test material occurred. The measured concentrations likely do not represent the

actual concentrations to which the organisms were exposed.

#### 10 SUBMISSION PURPOSE:

# 11. MATERIALS AND METHODS:

# A. Test Organisms/Acclimation:

Guideline Criteria	Reported Information
<u>Species</u> Daphnia magna	Daphnia magna
Source	In-house culture
Parental Acclimation Conditions Parental stock must be maintained separately from the brood culture in dilution water and under test conditions.	Daphnid cultures were maintained under similar conditions as those used during the test.
Parental Acclimation Period At least 21 days.	Not reported
Age of Parental Stock At least 10-12 days old at the beginning of the acclimation period.	At least 14 days
Food Synthetic foods (trout chow), algae, or synthetic foods in combination with alfalfa yeast and algae.	Ankistrodesmus convolutus
Food Concentration 5 mg/l (dry wt.) of synthetic food or 10 cells/l of algae is recommended.	20 ml (per replicate) of algal suspension twice daily
Were daphnids in good health during acclimation period?	Yes

#### B. Test System:

Guideline Criteria	Reported Information
Test Water Unpolluted well or spring that has been tested for contaminants, or appropriate reconstituted water (see ASTM for details).	Filtered, sterilized municipal water that has been tested for contaminants.
Water Temperature 20°C ±2°C. Must not deviate from 20°C by more than 5°C for more than 48 hours.	19.6 - 21.0°C
<pre>pH 7.6 to 8.0 is recommended. Must not deviate by more than one unit for more than 48 hours.</pre>	7.0 - 7.7
Total Hardness 160 to 180 mg/l as CaCO3 is recommended.	61 - 76 mg/l as CaCO <sub>3</sub>
Dissolved Oxygen  Renewal: must not drop below 50% for more than 48 hours.  Flow-through: ≥ 60% throughout test.	Mean of >76% of saturation throughout the test
Test Vessels or Compartments  1. Material: Glass, No. 316 stainless steel, or perfluorocarbon plastics  2. Size: 250 ml with 200 ml fill volume is preferred; 100 ml with 80 ml fill volume is acceptable.	1. Glass  2. 600-mL filled to approximately 525 mL
Covers Renewal: Test vessels should be covered with a glass plate. Flow-through: openings in test compartments should be covered with mesh nylon or stainless steel screen.	Not reported

Guideline Criteria	Reported Information
Type of Dilution System  Must provide reproducible supply of toxicant.  Intermittent flow proportional diluters or continuous flow serial diluters should be used.	Intermittent-flow proportional diluter
Flow Rate Consistent flow rate of 5-10 vol/24 hours, meter systems calibrated before study and checked twice daily during test period.	6 volume replacements/24 hours
Aeration Dilution water should be vigorously aerated, but the test tanks should not be aerated.	Test vessels were not aerated during test.
<pre>Photoperiod 16 hours light, 8 hours dark.</pre>	16 hours light, 8 hours dark
Solvents Not to exceed 0.5 mL/l for static tests or 0.1 mL/l for flow-through tests. Acceptable solvents are dimethyl formamide, triethylene glycol, methanol, acetone and ethanol.	Solvent: acetone Maximum conc.: 0.1 mL/L

# C. Test Design:

Guideline Criteria	Reported Information
<u>Duration</u> 21 days	21 days
Nominal Concentrations Control(s) and at least 5 test concentrations; dilution factor not greater than 50%.	Dilution water control, solvent control and 6 nominal concentrations: $78.0$ , $130$ , $216$ , $360$ , $600$ , and $1000 \mu g/L$

Guidallina Guitauria	Danasta 2 Tabanmatan
Guideline Criteria  Number of Test Organisms  22 daphnids/level;  7 test chambers should contain  1 daphnid each, and 3 test chambers should contain 5 daphnids each.	Reported Information  5 daphnids/replicate; 4 replicates per treatment and control
Test organisms randomly or impartially assigned to test vessels?	Yes
Renewal Parent daphnids in all beakers must be transferred to containers with fresh test solution (< 4 hours old) three times each week (e.g. every Monday, Wednesday and Friday).	N/A
Water Parameter Measurements  1. Dissolved oxygen must be measured at each concentration at least once a week.  2. pH, alkalinity, hardness, and conductance must be measured once a week in one test concentration and in one control.  3. Temperature should be monitored at least hourly throughout the test in one test chamber, and near the beginning, middle and end of the test in all test chambers.	<ol> <li>D.O. and pH were measured weekly in each replicate including the controls</li> <li>Alkalinity, hardness, and conductivity were measured weekly in the controls and in the highest concentration with surviving daphnids.</li> <li>Temperature was measured continuously in one replicate vessel, and weekly in all treatment and control vessels.</li> </ol>
Chemical Analysis Needed if chemical was volatile, insoluble, or known to absorb, if precipitate formed, if containers were not steel or glass, or if flow- through system was used.	Parent compound was measured in each replicate on Days 0, 7, 14, and 21.

Other Applicable Information: Percent recoveries of the parent compound, fluroxypyr 1-metylheptyl ester (fluroxypyr 1-MHE), in treatment solutions ranged from 46.5 to 50.5% of nominal values. The low recoveries are primarily due to fluroxypyr 1-MHE rapidly hydrolyzing to fluroxypyr acid in water.

# 12. REPORTED RESULTS:

## A. General Results:

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes
Control Mortality ≤ 30%	0% in both the dilution water and solvent control
Did daphnids in each control produce at least 40 young after 21 days?	Yes
Were any ephippia produced in any of the controls?	No ephippia observed
<ul> <li>Data Endpoints</li> <li>Survival of first-generation daphnids,</li> <li>Number of young produced per female,</li> <li>Dry weight (required) and length (optional) of each first generation daphnid alive at the end of the test,</li> <li>Observations of other effects or clinical signs.</li> </ul>	<ul> <li>Survival of first-generation daphnids,</li> <li>Number of young produced per female,</li> <li>Day to first eggs</li> <li>Day to first brood</li> <li>Length of surviving first-generation daphnids,</li> <li>Clinical observations.</li> </ul>
Raw data included?	Yes

## Effects Data

Concer	icant tration g/L) Mean Measured	# dead daphnids/ total (%)	Mean Number Young per Female	Mean Total Length (mm)
Control	·	0/20 (0%)	65	3.72
Solvent Control		0/20 (0%)	78	3.89

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Concen	icant tration g/L) Mean Measured	# dead daphnids/ total (%)	Mean Number Young per Female	Mean Total Length (mm)
78.0	37.7	1/20 (5%)	81	3.98
130	60.5	0/20 (0%)	83	4.06
216	109	2/20 (10%)	. 57ª	3.98
360	174	1/20 (5%)	. 52ª	3.23
600	294	3/20 (15%)	30 <sup>a</sup>	3.43
1000	499	11/20 (55%)	7ª	3.06

a Significantly different from the pooled controls (p  $\leq 0.05$ ).

Toxicity Observations: None

B. Statistical Results: Analyses were based on mean response values compared to the pooled control.

Endpoint	Method	NOEC (μg/L)	LOEC (µg/L)
Young per adult	Dunnett's test	60.5	109
Length	Dunnett's test	499	>499

13. <u>VERIFICATION OF STATISTICAL RESULTS</u>: Analyses were made using mean response values compared to the solvent control.

Endpoint	Method	NOEC (ppb)	LOEC (ppb))
Survival	Williams' test	294	499
Young per adult	Dunnett's test	60.5	109
Young/adult/ reproductive day	Dunnett's test	109	174
Length	Dunnett's test	1.09.	174

14. <u>REVIEWER'S COMMENTS</u>: Statistical analysis was performed on both the total number of young produced per adult and on the mean young/adult/reproductive day. The total number of young produced per adult proved to be a more sensitive analysis (lower NOEC) than mean young/adult/reproductive day. Therefore, the reviewer chose the former analysis to represent the most sensitive parameter (reproduction) for this test.

This study is scientifically sound but does not fulfill the guideline requirements for a freshwater invertebrate lifecycle test using Daphnia magna. Testing was conducted at above the solubility limit. It is likely that there was some undissolved test material in the system, this was not reported. Also, by placing the samples in acetonitrile, any suspended particles would have dissolved and the actual test concentrations to which the organisms were exposed is unknown. It is likely that the reported measured concentrations are an overestimate. This study is classified as Supplemental.



# UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460

#### **MEMORANDUM**

SUBJECT: Data Evaluation Records for Fluroxypyr (Chemical # 128959) and

Fluroxypyr 1-methylheptyl ester (Chemical # 128968), ID # 062719-EIL

Micholas Mastro

STARANE F, Case # 060640, Bar Code # D231718

FROM:

F. Nicholas Mastrota

Environmental Risk Branch II

Environmental Fate and Effects Division 7507C

THRU:

Elizabeth M. Leovey, Chief

Environmental Risk Branch II

Environmental Fate and Effects Division 7507C

TO:

Joanne Miller (23)

Registration Division (7505C)

EFED has completed review of seven ecological effects studies for fluroxypyr (chemical # 128959) and fluroxypyr 1-methylheptyl ester (chemical # 128968). Two of these studies were unacceptable for fulfilling guideline requirements. The aquatic plant study testing the effects of fluroxypyr 1-methylheptyl on *Navicula pelliculosa* (Guideline 123-2, MRID 440803-39) is invalid because the solvent control was contaminated with the test material. This study may be upgraded if the registrant submits data for the solvent control (if it exists) and these data are judged to be adequate for data analysis. The study testing the effects of fluroxypyr 1-methylheptyl on the shell deposition of oysters (Guideline 72-3b, MRID 440803) is supplemental because suspended insoluble test material was apparent solutions at the three highest test concentrations. This study cannot be repaired. The other five studies were classified as core and fulfil the guideline requirements.

#### Summary of Data Reviews

Guideline	Study Type	Test Species	MRID	Acceptability
	Fluroxypyr			
72-3(a)	Estuarine/marine fish LC <sub>50</sub>	Silverside	440803-09	Core
72-3(b)	Estuarine/marine mollusk LC <sub>50</sub>	Eastern Oyster	440803-11	Core
72-3(c)	Estuarine/marine shrimp LC <sub>50</sub>	Grass shrimp	440803-12	Core
	Fluroxypyr 1-methylheptyl ester			
72-3(a)	Estuarine/marine fish LC <sub>50</sub>	Sheepshead minnow	440803-08	Core
72-3(b)	Estuarine/marine mollusk LC <sub>50</sub>	Eastern oyster	440803-10	Supplemental
72-3(c)	Estuarine/marine shrimp LC <sub>50</sub>	Grass shrimp	440803-13	Core
123-2	Aquatic plant LC <sub>50</sub>	Freshwater diatom ( <i>Navicula</i> <i>pelliculosa)</i>	440803-39	Invalid

#### **DER Conclusions**

MRID 440803-08: This study is scientifically sound and fulfills the guideline requirements. The 96-hour  $LC_{50}$  for sheepshead minnow was determined to be >0.087 ppm (>100 ppm nominal), which classifies fluroxypyr 1-methylheptyl ester as practically non-toxic to the sheepshead minnow (i.e., it is non-toxic at its solubility limit).

MRID 440803-09: This study is scientifically sound and fulfills the guideline requirements. The 96-hour  $LC_{50}$  was determined to be 40 ppm, which classifies fluroxypyr as slightly toxic to the silverside.

MRID 440803-10: Because insoluble test material was present in the test solutions, this study is classified as supplemental. The 96-hour  $EC_{50}$  for oyster shell deposition was determined to be 68 ppb, which classifies the test material as very highly toxic to the eastern oyster. The NOEC could not be determined due to treatment-related reductions in shell deposition at all levels. These results may overestimate the toxicity

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of fluroxypyr 1-methylheptyl ester and thus should only be used as part of a conservative screen of risk to marine/estuarine mollusks.

MRID 440803-11: This study is scientifically sound and fulfills the guideline requirements. A 96-hour  $EC_{50}$  of 51 ppm classifies fluroxypyr as slightly toxic to the eastern oyster. The NOEC was 16 ppm.

MRID 440803-12: This study is scientifically sound and fulfills the guideline requirements. The 96-hour  $LC_{50}$  for grass shrimp was determined to be > 120 ppm, which classifies fluroxypyr as practically non-toxic to the grass shrimp.

MRID 440803-13: This study is scientifically sound and fulfills the guideline requirements. The 96-hour  $LC_{50}$  was determined to be >0.135 ppm (>100 ppm nominal), which classifies the 1-methylheptyl ester of fluroxypyr as practically nontoxic to the grass shrimp (i.e., it is nontoxic at its solubility limit).

MRID 440803-39: This study is not scientifically sound and does not fulfill the guideline requirements for an algal toxicity test. The solvent control solutions were contaminated with test material. Negative control data were not included in the report. This data could be upgraded if the negative control data (if it exists) is submitted to the Agency.

Please forward copies of the DERs to the registrant as soon as possible. The information requested for MRID 440803-39 is needed to complete the Section 3 ecological risk assessment.

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#### DATA EVALUATION RECORD § 72-3 - ACUTE LC<sub>50</sub> TEST WITH AN ESTUARINE/MARINE FISH

128968

CHEMICAL: Fluroxypyr 1.

PC Code No.: 128959

TEST MATERIAL: Fluroxypyr 1-methylheptyl ester Purity: 95.8% 2.

3. CITATION:

> Authors: R.L. Boeri, P.L. Kowalski, and T.J. Ward

Fluroxypyr 1-Methylheptyl Ester: Acute Title:

Toxicity to the Sheepshead Minnow,

Cyprinodon variegatus

January 15, 1996 Study Completion Date:

Laboratory: T.R. Wilbury Laboratories, Inc.,

Marblehead, MA

The Dow Chemical Company, Midland, MI Sponsor:

Laboratory Report ID: 707-DO

440803-08 MRID No.: DP Barcode: D231718

REVIEWED BY:

Mark Mossler, M.S., Toxicologist, KBN Engineering and Applied Sciences, Inc.,

Signature: /

Date:

Max Feken, M.S., Environmental Toxicologist, APPROVED BY:

KBN Engineering and Applied Sciences, Inc.,

APPROVED BY: F. Nicholas Mastrota, ERBII, EFED

J. Nicholas Montenter Date:

Signature:

STUDY PARAMETERS:

Age or Size of Test Organism:

25 mm

Definitive Test Duration:

96 hours

Study Method:

Flow-through

Type of Concentrations:

Mean measured

**CONC!JUSIONS:** This study is scientifically sound and fulfills the guideline requirements. The 96-hour LC<sub>50</sub> for sheepshead minnow was determined to be >0.087 ppm (>100 ppm nominal), which classifies fluroxypyr 1-methylheptyl ester as practically non-toxic to the sheepshead minnow, (ie., it is nontoxic at its solubility limit). In M

Results Synopsis:

 $LC_{50}$ : >0.087 ppm (>100 ppm nominal)

95% C.I.: N/A

NOEC: 0.087 ppm (100 ppm nominal)

Probit Slope: N/A

# 8. ADEQUACY OF THE STUDY:

A. Classification: Core

B. Rationale: N/A

C. Repairability: N/A

9. <u>GUIDELINE DEVIATIONS</u>: The length range of the control fish at test termination was not reported.

#### 10. SUBMISSION PURPOSE:

#### 11. MATERIALS AND METHODS:

## A. Test Organisms

Guideline Criteria	Reported Information
Species Preferred species are the sheepshead minnow (Cyprinodon variegatus) or the Silverside (Menidia sp.)	Cyprinodon variegatus
Mean Weight 0.5-5 g	0.24 g
Mean Standard Length Longest not > 2x shortest	Mean: 25 mm Range: Not reported
Supplier	Aquatox, Inc., Hot Springs, AR
All fish from same source?	Yes
All fish from the same year class?	Yes

#### B. Source/Acclimation

Guideline Criteria	Reported Information
<u>Acclimation Period</u> Minimum 14 days	Held under conditions similar to testing for one month
Wild caught organisms were quarantined for 7 days?	N/A
Were there signs of disease or injury?	No

Guideline Criteria	Reported Information
If treated for disease, was there no sign of the disease remaining during the 48 hours prior to testing?	N/A
<u>Feeding</u> No feeding during the study	Last fed 48 hours prior to testing
<pre>Pretest Mortality &lt; 3% mortality 48 hours prior to testing</pre>	No mortality in the 48 hours prior to testing

# C. Test System

Guideline Criteria	Reported Information
Source of dilution water Soft reconstituted water or water from a natural source, not dechlorinated tap water	Seawater collected from the Atlantic Ocean was adjusted to a salinity of 11-17 parts per thousand. The water was aerated, filtered, and UV sterilized.
Does water support test animals without observable signs of stress?	Yes
Salinity 30-34 % salinity, weekly range <6 %	15-16 ‰
Water Temperature 22 <u>+</u> 1 °C	22.1-22.8°C
<pre>pH 8.0-8.3 for marine-stenohaline fishes, 7.7-8.0 for estuarine- euryhaline fishes, monthly range &lt; 0.8</pre>	7.6-8.0
Dissolved Oxygen Static: ≥ 60% during 1 <sup>st</sup> 48 hrs and ≥ 40% during 2 <sup>nd</sup> 48 hrs, flow-through: ≥ 60%	≥78% saturation during the test



Guideline Criteria	Reported Information
Test Aquaria  1. Material:     Glass or stainless steel  2. Size:     Volume of 19 L (5 gal) or     30 x 60 x 30 cm  3. Fill volume:     15-30 L of solution	Glass 20-L 15 L
Type of Dilution System  Must provide reproducible supply of toxicant	Intermittent-flow proportional diluter
Flow Rate Consistent flow rate of 5-10 vol/24 hours, meter systems calibrated before study and checked twice daily during test period	7.0 volume replacements/24 hr
Biomass Loading Rate Static: ≤ 0.8 g/L at ≤ 17°C, ≤ 0.5 g/L at > 17°C; flow- through: ≤ 1 g/L/day	0.034 g/L/day
<pre>Photoperiod 16 hours light, 8 hours dark</pre>	16 h light, 8 h dark
Solvents Not to exceed 0.5 mL/L for static tests or 0.1 mL/L for flow-through tests	Solvent: DMF Maximum conc.: 0.5 mL/L

# D. Test Design

Guideline Criteria	Reported Information
Range Finding Test If $LC_{50} > 100$ mg/L with 30 fish, then no definitive test is required.	Yes; 0.010, 0.10, 1.0, and 10 mg/L. After 96 hours, no mortality was observed at any concentration. Insoluble material was observed at 1.0 and 10 mg/L.

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Guideline Criteria	Reported Information		
Nominal Concentrations of Definitive Test Control & 5 treatment levels; dosage should be 60% of the next highest concentration; concentrations should be in a geometric series	Control, solvent control, and 100 mg/L, corrected for purity		
Number of Test Organisms Minimum 10/level, may be di- vided among containers	30 fish per treatment level and controls, 15 per replicate vessel		
Test organisms randomly or impartially assigned to test vessels?	Yes		
Biological observations made every 24 hours?	Yes		
Water Parameter Measurements  1. Temperature  Measured constantly or, if water baths are used, every 6 hrs, may not vary > 1°C	Temperature measured continuously in one test chamber and daily in each chamber		
2. <u>DO and pH</u> Measured at beginning of  test and ever 48 h in the  high, medium, and low doses  and in the control	DO and pH measured daily in each chamber		
Chemical Analysis Needed if solutions were aerated, if chemical was volatile, insoluble, or known to absorb, if precipitate formed, if containers were not steel or glass, or if flow- through system was used	Solutions were collected from each replicate at test initiation, 48 hours after initiation, and termination. Alternate replicate samples were filtered and analyzed by HPLC. The other replicate sample was stored as back-up.		

# 12. REPORTED RESULTS:

# A. General Results

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes



Guideline Criteria Reported Information					
Recovery of Chemical	<1% of nominal				
Control Mortality Not more than 10% control organisms may die or show abnormal behavior.	No mortality in any group				
Raw data included?	Yes				
Signs of toxicity (if any) were described?	No signs of toxicity observed				

#### Mortality

Concentrati	Concentration (ppm) Cumulative Number Dead					Dead
	Mean	Number of Fish		6-68-88 13 A - 88	Study	
Nominal	Measured	1.1511	24	4.8	72	96.
Control	<0.025	30	0	0	0	0
Sol. Con.	<0.025	30	0	0	0	0
100	0.087.	30	0	О	0	0

Other Significant Results: Particulate matter was observed in the treatment solution.

#### B. Statistical Results

Method: Visual interpretation

96-hr LC<sub>50</sub>: >0.087 ppm 95% C.I.: N/A Probit Slope: N/A NOEC: 0.087 ppm

- 13. VERIFICATION OF STATISTICAL RESULTS: The lack of mortality precluded the use of regression analysis to determine the  $LC_{50}$ . It is apparent that the 96-hour  $LC_{50}$  is greater than the maximum saltwater solubility of the test material.
- 1.4. REVIEWER'S COMMENTS: The test material was supplied to the aquaria at a concentration of 100 ppm. However, the test material was reported to be soluble in water only to a concentration of 100 ppb (at 25°C). The authors used solvent (DMF; 0.5 mL/L) to dissolve the test substance and a high shear pump to mix the treatment solution. It is therefore apparent that every effort was made to solubilize the test material in saltwater. Consequently, this study is

scientifically sound and can be classified as <code>Core</code>. The 96-hour  $LC_{50}$  for sheepshead minnow was determined to be >100 ppm (>0.087 ppm mean measured), which classifies the test material as practically non-toxic to the sheepshead minnow. The NOEC was 100 ppm (0.087 ppm mean measured).

#### DATA EVALUATION RECORD § 72-3 - ACUTE LC<sub>50</sub> TEST WITH AN ESTUARINE/MARINE FISH

1. CHEMICAL: Fluroxypyr PC Code No.: 128959

2. TEST MATERIAL: Fluroxypyr Purity: 98.7%

3. CITATION:

Authors: R.L. Boeri, P.L. Kowalski, and T.J. Ward

Title: Fluroxypyr: Acute Toxicity to the

Silverside, Menidia beryllina

Study Completion Date: February 4, 1994

Laboratory: T.R. Wilbury Laboratories, Inc.,

Marblehead, MA

Sponsor: The Dow Chemical Company, Midland, MI

<u>Laboratory Report ID</u>: 199-DO

MRID No.: 440803-09
DP Barcode: D231718

4. REVIEWED BY: Mark Mossler, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.,

Signature: Mathinster D

Date: 6/17/17

APPROVED BY: Max Feken, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.,

Signature: // hole

Date: 6/17/97

5. APPROVED BY: F. Nicholas Mastrota, Wildlite Biologist, ERBIT, EFED

Signature: J. Micholas Mastata Date: 6/29/97

6. STUDY PARAMETERS:

Age or Size of Test Organism: 40 mm

Definitive Test Duration: 96 hours

Study Method: Flow-through

Type of Concentrations: Mean measured

7. <u>CONCLUSIONS</u>: This study is scientifically sound and fulfills the guideline requirements. The 96-hour LC<sub>50</sub> was determined to be 40 ppm, which classifies fluroxypyr as slightly toxic to the silverside.

#### Results Synopsis:

LC<sub>50</sub>: 40 ppm

NOEC: Not determined

95% C.I.: 27-47 ppm

Probit Slope: N/A

#### 8. ADEQUACY OF THE STUDY:

A. Classification: Core

B. Rationale: N/A

C. Repairability: N/A

9. <u>GUIDELINE DEVIATIONS</u>: The length range of the control fish at test termination was not reported.

#### 10. SUBMISSION PURPOSE:

#### 11. MATERIALS AND METHODS:

#### A. Test Organisms

Guideline Criteria	Reported Information
<u>Species</u> Preferred species are the sheepshead minnow ( <i>Cyprinodon variegatus</i> ) or the silverside ( <i>Menidia sp.</i> ).	Menidia beryllina
Mean Weight 0.5-5 g	0.39 g
<u>Mean Standard Length</u> Longest not > 2x shortest	Mean: 40 mm Range: Not reported
Supplier	Aquatic Biosystems, Inc., Fort Collins, CO
All fish from same source?	Yes
All fish from the same year class?	Yes, approximately 6.5 to 7.5 months old

#### B. Source/Acclimation

Guideline Criteria	Reported Information
Acclimation Period Minimum 14 days	Held under similar conditions to testing for 2.5 months
Wild caught organisms were quarantined for 7 days?	N/A

Guideline Criteria	Reported Information
Were there signs of disease or injury?	No
If treated for disease, was there no sign of the disease remaining during the 48 hours prior to testing?	N/A
<u>Feeding</u> No feeding during the study	Last fed 48 hours prior to testing
<pre>Pretest Mortality &lt; 3% mortality 48 hours prior to testing</pre>	Less than 3% mortality in the 48 hours prior to testing

## C. Test System

Guideline Criteria	Reported Information
Source of dilution water Soft reconstituted water or water from a natural source, not dechlorinated tap water	Seawater collected from the Atlantic Ocean was adjusted to a salinity of 11-17 parts per thousand. The water was aerated, filtered, and UV sterilized.
Does water support test animals without observable signs of stress?	Yes
Salinity 30-34 % salinity, weekly range <6 %	17 ‰
Water Temperature 22 ± 1 °C	21.3-22.3°C
<pre>pH 8.0-8.3 for marine-stenohaline fishes, 7.7-8.0 for estuarine- euryhaline fishes, monthly range &lt; 0.8</pre>	7.5-7.9
<u>Dissolved Oxygen</u> Static: $\geq$ 60% during 1 <sup>st</sup> 48 hrs and $\geq$ 40% during 2 <sup>nd</sup> 48 hrs, flow-through: $\geq$ 60%	≥97% saturation during the test

Guideline Criteria	Reported Information
Test Aquaria  1. Material:     Glass or stainless steel  2. Size:     Volume of 19 L (5 gal) or     30 x 60 x 30 cm  3. Fill volume:     15-30 L of solution	Glass 20-L 15 L
Type of Dilution System Must provide reproducible supply of toxicant	Intermittent-flow proportional diluter
Flow Rate Consistent flow rate of 5-10 vol/24 hours, meter systems calibrated before study and checked twice daily during test period	5.4 volume replacements/24 hr
Biomass Loading Rate Static: ≤ 0.8 g/L at ≤ 17°C, ≤ 0.5 g/L at > 17°C; flow- through: ≤ 1 g/L/day	0.05 g/L/day
<pre>Photoperiod 16 hours light, 8 hours dark</pre>	16 h light, 8 h dark
Solvents Not to exceed 0.5 mL/L for static tests or 0.1 mL/L for flow-through tests	Solvent: none Maximum conc.: N/A

## D. Test Design

Guideline Criteria Reported Information		
Range Finding Test  If LC <sub>50</sub> >100 mg/L with 30 fish, then no definitive test is required.	Test concentrations were selected based upon 3 tests which produced mortality of 0% at concentrations <100 ppm and 100% at concentrations ≥100 ppm.	

Guideline Criteria	Reported Information
Nominal Concentrations of Definitive Test Control & 5 treatment levels; dosage should be 60% of the next highest concentration; concentrations should be in a geometric series	Control, 18, 30, 48, 72, and 120 mg/L, corrected for purity
Number of Test Organisms Minimum 10/level, may be di- vided among containers	20 fish per treatment or control group, 10 per replicate vessel
Test organisms randomly or impartially assigned to test vessels?	Yes
Biological observations made every 24 hours?	Yes
<pre>Water Parameter Measurements 1. Temperature    Measured constantly or, if    water baths are used, every    6 hrs, may not vary &gt; 1°C 2. DO and pH    Measured at beginning of    test and ever 48 h in the    high, medium, and low doses</pre>	Temperature measured at least every six hours in one test chamber and daily in each chamber that contained live fish  DO and pH measured daily in each chamber that contained
and in the control	live fish
Chemical Analysis Needed if solutions were aerated, if chemical was volatile, insoluble, or known to absorb, if precipitate formed, if containers were not steel or glass, or if flow- through system was used	Solutions collected from pooled replicate samples at test initiation, 48 hours after initiation, and termination were filtered and analyzed by HPLC.

#### 12. REPORTED RESULTS:

#### A. General Results

Guideline Criteria	. Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes

Guideline Criteria	Reported Information
Recovery of Chemical	89-100% of nominal
Control Mortality Not more than 10% control organisms may die or show abnormal behavior.	Five percent mortality in the control group
Raw data included?	Yes
Signs of toxicity (if any) were described?	Yes, signs of toxicity observed at all treatment levels

Mortality

Concentration (ppm)			Cumulative Number Dead			
		Number of		Hour o	f Study	
Nominal	Mean Measured	Fish	24	48	72	96
Control	<1.0	20	0	0	1	1
18	16	20	0	0	0	0
30	27	20	0	0	0	0
48	47	20	0	3	13	16
72	69	20	14	20	20	20
120	120	20	20	20	20	20

Other Significant Results: Signs of toxicity including erratic swimming and loss of equilibrium were noted in all treatment groups containing live fish at 72 and 96 hours after initiation.

#### B. Statistical Results

Method: Nonlinear interpolation/binomial probability

96-hr LC<sub>50</sub>: 40 ppm 95% C.I.: 27-47 ppm

Probit Slope: N/A NOEC: <16 ppm

#### 13. VERIFICATION OF STATISTICAL RESULTS:

Method: Binomial probability

96-hr LC<sub>50</sub>: 40 ppm 95% C.I.: 27-47 ppm Probit Slope: N/A NOEC: Not determined

14. REVIEWER'S COMMENTS: This study is scientifically sound, fulfills the guideline requirements, and can be classified as Core. The 96-hour LC<sub>50</sub> was determined to be 40 ppm, which classifies the test material as slightly toxic to the silverside. The NOEC could not be determined due to treatment-related effects at all concentrations.

NOTE: THERE WAS CONTROL MORTALITY, BUT AT LEAST ONE OF THE LOWER CONCENTRATIONS HAD ZERO MORTALITY. THEREFORE, ABBOTT'S CORRECTION IS NOT APPLICABLE.

MOSSLER FLUROXYPYR Menidia beryllina 6-2-97

CONC.	NUMBER	NUMBER	PERCENT	BINOMIAL PROB. (PERCENT)
	EXPOSED	DEAD	DEAD	
120	20	20	100	9.536742E-05
69	20	20	100	9.536742E-05
47	20	16	80	.5908966
27	20	0	0	9.536742E-05
16	20	0	0	9.536742E-05

THE BINOMIAL TEST SHOWS THAT 27 AND 47 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 39.5599

WHEN THERE ARE LESS THAN TWO CONCENTRATIONS AT WHICH THE PERCENT DEAD IS BETWEEN 0 AND 100, NEITHER THE MOVING AVERAGE NOR THE PROBIT METHOD CAN GIVE ANY STATISTICALLY SOUND RESULTS.

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# DATA EVALUATION RECORD § 72-3 - ACUTE EC<sub>50</sub> TEST WITH AN ESTUARINE/MARINE MOLLUSK SHELL DEPOSITION STUDY

L. <u>CHEMICAL</u>: Fluroxypyr <u>PC Code No.</u>: 128968

2. TEST MATERIAL: Fluroxypyr 1-methylheptyl ester Purity: 95.8%

3. CITATION:

Authors: R.L. Boeri, P.L. Kowalski, and T.J. Ward

Title: Fluroxypyr 1-Methylheptyl Ester: Acute

Flow-Through Mollusc Shell Deposition

Test ·

Study Completion Date: January 12, 1996

Laboratory: T.R. Wilbury Laboratories, Inc.,

Marblehead, MA

Sponsor: The Dow Chemical Company, Midland, MI

<u>Laboratory Report ID</u>: 646-DO

MRID No.: 440803-10

DP\_Bar Code: D231718

4. REVIEWED BY: F. Nicholas Mastrota, ERB II, EFED, EPA

Signature: F. Nicholas Mostooto Date: 7-28-97

5. PEER REVIEWED BY: Andrew Bryceland, ERB II, EFED, EPA

6. STUDY PARAMETERS:

Age or Size of Test Organism: Valve height, 26-40 mm

Definitive Test Duration: 96 hours

Study Method: Flow-through

Type of Concentrations: . Mean measured

7. <u>CONCLUSIONS</u>: Because insoluble test material was present in the test solutions, this study is classified as supplemental. The 96-hour  $EC_{50}$  for oyster shell deposition was determined to be 68 ppb, which classifies the test material as very

highly toxic to the eastern oyster. The NOEC could not be determined due to treatment-related reductions in shell deposition at all levels. These results may overestimate the toxicity of fluroxypyr 1-methylheptyl ester and thus should only be used as part of a conservative screen of risk to marine/estuarine mollusks.

#### 8. ADEQUACY OF THE STUDY:

- A. Classification: Supplemental.
- B. Rationale: The three highest test solutions were cloudy throughout the test, indicating that insoluble test material was present in the water column. This insoluble material may have contributed to the observed reduction in shell deposition.
- C. Repairability: Not repairable.
- 9. <u>GUIDELINE DEVIATIONS</u>: Solutions in the test chambers at the three highest concentrations were cloudy throughout the test, indicating that insoluble test material was present in the water column.
- 10. SUBMISSION PURPOSE: New chemical registration.

#### 11. MATERIALS AND METHODS:

#### A. Test Organisms

Guideline Criteria	Reported Information
Species Pieferred species are the Pacific oyster (Crassostrea gigas) and the Eastern oyster (Crassostrea virginica)	Crassostrea virginica
Mean valve height 25 - 50 mm along the long axis	26 - 40 mm

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Guideline Criteria	Reported Information
Supplier	P. Cummins Oyster Co., Pasadena, MD
Are all oysters from same source?	Yes
Are all oysters from the same year class?	Reported as juvenile

## B. Source/Acclimation

Guideline Criteria	Reported Information
Acclimation Period  Minimum 10 days after  collection	Acclimated for 10 days prior to testing
Wild caught organisms were quarantined for 7 days?	N/A
Were there signs of disease or injury?	No
If treated for disease, was there no sign of the disease remaining during the 48 hours prior to testing?	N/A
Amount of peripheral shell growth removed prior to testing	3-5 mm
Feeding during the acclimation Must be fed to avoid stress.	Live marine phytoplankton added to unfiltered seawater
<pre>Pretest Mortality &lt;3% mortality 48 hours prior to testing</pre>	No mortality during the 48 hours prior to testing

## C. Test System

Guideline Criteria	Reported Information						
Source of dilution water Natural unfiltered seawater from an uncontaminated source	Unfiltered, aerated seawater collected from the Atlantic Ocean						
Does water support test animals without observable signs of stress?	Yes						
Salinity 30-34 % salinity, weekly range	33 %						
Water Temperature 15-30°C, consistent in all test vessels	20.7-21.4°C						
Hg	7.7-8.0						
Dissolved Oxygen ≥ 60% throughout	≥64% of saturation throughout the test						
Total Organic Carbon	Not reported						
Test Aquaria Should be constructed of glass or stainless steel	Glass aquaria were 20-L in volume containing 15 L of dilution water						
Type of Dilution System  Must provide reproducible supply of toxicant	Intermittent-flow proportional diluter						
Flow rate Consistent flow rate	9.8 volume replacements/24 hr						
Was the loading of organism such that each individual sits on the bottom with water flowing freely around it?	Yes						
<u>Photoperiod</u> 16 hours light, 8 hours dark	16 hours light, 8 hours dark						
Solvents Not to exceed 0.5 ml/L	Solvent: DMF Maximum conc.: 0.5 mL/L						

#### D. Test Design

Guideline Criteria	Reported Information
Range Finding Test  If EC <sub>50</sub> >100 mg/L with 30 oysters, then no definitive test is required	Concentrations selected for the definitive test were based on the results of six previous tests.
Nominal Concentrations of Definitive Test Control & 5 treatment levels; each conc. should be 60% of the next highest conc.; concentrations should be in a geometric series	Control, solvent control, 12, 20, 32, 48, and 80 mg/L, corrected for purity
Number of Test Organisms Minimum 20 individual per test level and in each control	20 oysters per treatment or control group
Test organisms randomly or impartially assigned to test vessels?	Yes
Biological observations made every 24 hours?	Yes
Water Parameter Measurements  1. Temperature Measured hourly in at least one chamber  2. DO and pH Measured at beginning of test and every 48 h in the high, medium, and low doses and in the control	Temperature was measured continuously in one vessel and daily in each chamber.  DO and pH were measured daily in each chamber.

Guideline Criteria	Reported Information
Was chemical analysis performed to determine the concentration of the test material at the beginning and end of the test? (Optional)	Replicate solutions were collected at initiation, 48 hours after initiation, and at test termination. Half of the samples were filtered and analyzed by HPLC, and half were kept as backup.

## 12. REPORTED RESULTS:

## A. General Results

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes
Control Mortality Not more than 10% of control organisms may die or show abnormal behavior	0%
Control Shell Deposition Must be at least 2 mm	Control - 2.3 mm Solvent Control - 2.4 mm
Recovery of Chemical	<1% of nominal
Raw data included?	Yes
Signs of toxicity (if any) were described?	Yes

	eration om)	Number		Mean Shell	Mean	
Nominal	Mean Measured	Per Level	Number Dead	Deposition (mm)	Percent Decrease'	
Control	<0.025	20	0	2.3		
Sol. Con.	<0.025	20	.0	. 2.4		
12	0.050	. 20 .	0	1.4	42	
20	0.063	20	0	1.3	46	
32	0.094	20	0	0.8	· 67	
48	0.127	20	0	0.7	71	
80.	0.167	·. 20	. 0	0.4	83	

<sup>\*</sup>Based on comparison to the solvent control.

Other Significant Results: No sublethal effects were noted in the control or treatment groups.

#### B. Statistical Results

Statistical method: Bonferroni's T-test was used for NOEC determination and weighted least-squares non-linear regression was used to determine the  $EC_{50}$  value. Treatment data were compared to the pooled control.

96-hr EC<sub>50</sub>: 0.096 ppm

95% C.I.: 0.051-0.179 ppm

Probit Slope: N/A NOEC: <0.050 ppm

#### 13. <u>VERIFICATION OF STATISTICAL RESULTS</u>:

Parameter	Result
Statistical Method for EC <sub>50</sub>	non-linear regression
EC <sub>50</sub> (95% C.I.)	68 ppb (52 - 90 ppb)
Probit Slope	N/A

Statistical Method for NOEC	Williams' Test
NOEC	Could not be determined

#### 14. REVIEWER'S COMMENTS:

In the definitive test, all nominal concentrations were over 100 times the solubility limit of fluroxypyr 1-methylheptyl ester. An excessive amount of test material was apparently added to the stock solution in order to achieve test concentrations near the solubility limit. The stock solution was proportionally diluted and mixed, and then was passed through a 5- $\mu$  filters before entering the test chambers. These filter were apparently too course to remove all of the insoluble test material because solutions in test vessels at the three highest concentrations were cloudy throughout the test. Since oysters are filter feeders, the presence of this insoluble material could have irritated the test organisms and contributed to the observed reduction of shell deposition.

The analysis of the test material was conducted with water samples that were filtered with  $0.45-\mu$  filter. This was likely sufficient to filter out most of the insoluble material. The reported test concentrations thus likely reflect only the soluble portion of the test material in the water column. Since the oysters were also exposed to insoluble material, the EC<sub>50</sub> calculated based on these measured concentrations is likely to overestimate the toxicity of dissolved test material.

Because insoluble test material was present in the test solutions, this study is classified as supplemental. The 96-hour  $EC_{50}$  for oyster shell deposition was determined to be 68 ppb, which classifies the test material as very highly toxic to the eastern oyster. The NOEC could not be determined due to treatment-related reductions in shell deposition at all levels. These results may overestimate the toxicity of fluroxypyr 1-methylheptyl ester (i.e., underestimate the  $EC_{50}$ ) and thus should only be used as part of a conservative screen of risk to marine/estuarine mollusks.

Oyster shell depo.

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WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Sol. Con.	20	2.350	2.350	2.350
2	50 ppb	20	1.445	1.445	1.445
3	63 ppb	20	1.265	1.265	1.265
4	94 ppb	20	0.820	0.820	0.820
5	127 ppb	20	0.745	0.745	0.745
6	167 ppb	20	0.420	0.420	0.420

Oyster shell depo.

File: oys Transform: NO TRANSFORMATION

 WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2 C	)F 2
 IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
 Sol. Con.	2.350				
50 ppb	1.445	5.316	*	1.67	k = 1, v = 114
63 ppb	1.265	6.373	*	1.75	k=2, v=114
94 ppb	0.820	8.987	*	1.77	k=3, v=114
127 ppb	0.745	9.428	*	1.78	k = 4, v = 114
167 ppb	0.420	11.337	*	1.79	k=5, v=114

s = 0.538

Note: df used for table values are approximate when v > 20.

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	38 39	0.050	-1.30103 -1.30103	5	0.9		}	103 104	0.167	-0.77728 -0.77728	į	1.5 0.6 0.0		
	40 41	0.050	-1.30103 -1.20066	1	0.9 1.2 1.7 2.5 1.2		}	105 106	0.167	-0.77728 -0.77728	1	1.0 0.6 0.0		
	43 44	0.063	-1.20066 -1.20066 -1.20066	1	1.6		}	101 102 103 104 105 106 107 108 109	0.167 0.167 0.167	-0.77728 -0.77728 -0.77728	1	1.2 0.0		
	45 46	0.063	-1.20066 -1.20066 -1.20066	1	1.2 1.0			110 111	0.167 0.167	-0.77728 -0.77728	1 2	0.0 0.7		
	47 48 49	0.063 0.063	-1.20066 -1.20066	1	0.8 2.5 1.0			111 112 113 114	0.167 0.167 0.167	-0.77728 -0.77728 -0.77728	5	0.0 0.0 0.0		
	10 112 13 145 17 189 190 122 122 122 122 123 123 123 123 123 123	0.000 0.000 0.000 0.000 0.000 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050	-1.20066 -1.20066 -1.20066	1 2	1.4 0.0		ŀ	115 116 117	0.094 0.094 0.094 0.094 0.094 0.094 0.094 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127 0.127	-1.02687 -1.02687 -1.02687 -1.02687 -1.02687 -1.02687 -1.02687 -1.02687 -1.02687 -1.02687 -1.02687 -1.02687 -1.02687 -1.02687 -1.02687 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.89620 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728 -0.77728	22222222	0.5 0.7		
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	55 56 57	0.063	-1.20066 -1.20066	2	1.3 1.9		}	120	0.167	-0.77728 shell depo.	Ž	1.0  4:46 Tuesday	, June 3,	1997
	57 58 59	0.063 0.063 0.063	-1.20066 -1.20066 -1.20066	5 5	0.6 0.8 0.9		MODEL:	: COUNT = C	U * PROI WEI	BNORM ((LOG E GHTED REGRESS	C50 - L	.OG_CONC) / S	IGMA)	
	60 61	0.063 0.094	-1.20066	2	0.9 1.3			Non-Li Dependent	near Le	ast Squares I e COUNT Met	terativ	iuss-Newton		
:	62 63 64	0.094 0.094	-1.02687 -1.02687 -1.02687	1	1.2 0.7			LOG EC50 -1.189000		SIGMA 0.342000	2.350	CO Weigh 2000 53.	ted SS 378245	
	65	0.094 0.094	-1.02687 -1.02687	1	0.9 0.8		1 2	-1.171766 -1.165665		0.441239 0.452703	2.351 2.348	37. 3405 36.	238006 159444	
•														

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File:A:oys.out Page 3 3 -1.165533 0.452825 2.348444 36.142522 4 -1.165533 0.452825 2.348444 36.142519 5 -1.165533 0.452825 2.348445 36.142519 NOTE: Convergence criterion met.	File:A:oys.out Page 4  LOWER Upper LOG EC25 -1.470959194 0.10135412837 -1.6716872435 -1.2702311442 SIGMA 0.452825307 0.07487227761 0.3045435696 0.6011070446 C0 2.348444501 0.18992353036 1.9723080723 2.7245809288
Non-Linear Least Squares Summary Statistics Dependent Variable COUNT	Asymptotic Correlation Matrix
Source DF Weighted SS Weighted MS	Corr LOG_EC25 SIGMA CO
Regression 3 140.90000000 46.96666667 Residual 117 36.14251916 0.30891042 Uncorrected Total 120 177.04251916	LOG EC25 1 -0.895926749 -0.655563239 51GMA -0.895926749 1 0.3719922286 C0 -0.655563239 0.3719922286 1 shell depo. 14:46 Tuesday, June 3, 1997
(Corrected Total) 119 70.69530358 .	MODEL: YOUNG = CO * PROBNORM ((LOG EC25 - LOG CONC) / SIGMA - 0.67449) SUMMARY OF NONLTHEAR REGRESSION
Parameter Estimate Asymptotic Asymptotic 95 %	OBS CONC LOG_EC25 SIGMA CO RESID_SS EC25
Std. Error Confidence Interval Lower Upper	1 0 -1.47096 0.45283 2.34844 36.1425 0.033810 shell depo. 14:46 Tuesday, June 3, 1997
LOG EC50 -1.165533052 0.06042737306 -1.2852071983 -1.0458589b66 \$1GMA    0.452825307 0.07487227761  0.3045435696  0.6011070446 C0    2.348444500 0.18992353036  1.9723080723  2.7245809287	MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
2.34044300 0.10372333030 1.7723000123 2.1723007201	Plot of COUNT*LOG CONC. Symbol used is '0'. Plot of PRED*LOG_CONC. Symbol used is '.'.
Asymptotic Correlation Matrix	COUNT
COFF LOG_EC50 SIGMA CO	4.5
LOG EC50 1 -0.667003548 -0.788685766 5IGMA -0.667003548 1 0.3719922286 C0 -0.788685766 0.3719922286 1 shell depo. 14:46 Tuesday, June 3, 1997 MODEL: COUNT = CO * PROBNORM ((LOG EC50 - LOG_CONC) / SIGMA)	
SUMMARY OF NONLINEAR REGRESSION	4.0
OBS CONC LOG_EC50 SIGMA CO RESID_SS EC50  1 0 -1.16553 0.45283 2.34844 36.1425 0.068307	
1 0 -1.16553 0.45283 2.34844 36.1425 0.068307 shell depo. 14:46 Tuesday, June 3, 1997 MODEL: YOUNG = CO * PROBNORM ((LOG EC25 - LOG CONC) / SIGMA - 0.67449) WEIGHTED REGRESSION	3.5
Non-Linear Least Squares Iterative Phase Dependent Variable COUNT Method: Gauss-Newton  Iter LOG EC25 SIGMA CO Weighted SS 0 -1.474000 0.342000 2.350000 84.891345 1 -1.520552 0.478203 2.355603 37.720954 2 -1.468972 0.452080 2.348641 36.052922 3 -1.470947 0.452818 2.348434 36.142409 4 -1.470959 0.452825 2.348444 36.142520 5 -1.470959 0.452825 2.348444 36.142519 6 -1.470959 0.452825 2.348444 36.142519	2.5 0
NOTE: Convergence criterion met.	
Non-Linear Least Squares Summary Statistics Dependent Variable COUNT	0
Source DF Weighted SS Weighted MS	2.0
Regression 3 140.90000000 46.96666667 Residual 117 36.14251916 0.30891042 Uncorrected Total 120 177.04251916	
(Corrected Total) 119 70.69530358	1.5 0 0 0 0
Parameter Estimate Asymptotic Asymptotic 95 % Std. Error Confidence Interval	0 0 0 0

File:A:oys.out   0   1.0 0   0	Page 5 0 0 0	•••••	0 0 0.	0 0 0	0	
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0.0	0		0	. 0	0	
-1.3	-1.2	-1.1	-1.0 LOG_CONC	-0.9	-0.8	-0.7

NOTE: 565 obs had missing values. 610 obs hidden.

shell depo. 14:46 Tuesday, June 3, 1997
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL

General Linear Models Procedure Class Level Information

Class Levels Values

DOSE 6 0 0.05 0.063 0.094 0.127 0.167

Number of observations in data set = 120

shell depo. 14:46 Tuesday, June 3, 1997
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL

General Linear Models Procedure

Dependent	Variable:	RESPONSE				•
Source		DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	•	5	46.85141667	9.37028333	32.33	0.0001
Error		114	33.03850000	0.28981140		•
Corrected	Total	119	79.88991667			
	R	-Square	c.v.	Root MSE	RESP	ONSE Mean
	0	.586450	45.84880	0.538341		1.174167
Source		DF	Type I SS	Mean Square	F Value	Pr > F
DOSE		5	46.85141667	9.37028333	32.33	0.0001
Source		DF	Type III SS	Mean Square	F Value	Pr > F
DOSE		5	46.85141667	9.37028333	32.33	0.0001

shell depo. 14:46 Tuesday, June 3, 1997 COMPARISON OF MEANS FOR NOEL DETERMINATION

|File:A:oys.out Page 6 | TEST IF TREATMENT IS LESS THAN CONTROL

#### General Linear Models Procedure

Level of		RESP	ONSE			
DOSE	N	Mean	SD			
0 0.05 0.063 0.094 0.127 0.167	20 20 20 20 20 20	2.35000000 1.44500000 1.26500000 0.82000000 0.74500000	0.66451407 0.34561159 0.59407159 0.48297325 0.59689989 0.48514783			
	_0	sheli depo.	14:46 Tuesday,	June	3,	1997

COMPARISON OF MEANS FOR NOEL DETERMINATION TEST IF TREATMENT IS LESS THAN CONTROL

General Linear Models Procedure

Dunnett's One-tailed T tests for variable: RESPONSE

NOTE: This tests controls the type I experimentwise error for comparisons of all treatments against a control.

Alpha= 0.05 Confidence= 0.95 df= 114 MSE= 0.289811 Critical Value of Dunnett's T= 2.260 Minimum Significant Difference= 0.3847

Comparisons significant at the 0.05 level are indicated by '\*\*\*'.

DOSE Comparison	Simultaneous Lower Confidence Limit	Difference Between Means	Simultaneou Upper Confidence Limit	-
0.05 - 0	-1,2897	-0.9050	-0.5203	***
0.063 - 0	-1.4697	-1.0850	-0.7003	***
0.094 - 0	-1.9147	-1.5300	-1.1453	***
0.127 - 0	-1.9897	-1.6050	-1.2203	***
0.167 - 0	-2.3147	-1.9300	-1.5453	***

#### DATA EVALUATION RECORD § 72-3 - ACUTE EC TEST WITH AN ESTUARINE/MARINE MOLLUSK SHELL DEPOSITION STUDY

128968

CHEMICAL: Fluroxypyr

PC Code No.: 128959

TEST MATERIAL: Fluroxypyr 1-methylheptyl ester Purity: 95.8%

3'. CITATION:

> R.L. Boeri, P.L. Kowalski, and T.J. Ward Authors: Fluroxypyr 1-Methylheptyl Ester: Acute Sitle: Flow-Through Mollusc Shell Deposition

Test

Study Completion Date: January 12, 1996

T.R. Wilbury Laboratories, Inc., Laboratory:

Marblehead, MA

The Dow Chemical Company, Midland, MI Sponsor:

Laboratory Report ID: 646-DO 440803-10 MRID No.:

D231718 DP Barcode:

Mark Mossler, M.S., Toxicologist, REVIEWED BY:

KBN Engineering and Applied Sciences, Inc.,

Signature: 6

Date: 6/17/97

Max Feken, M.S., Toxicologist, APPROVED BY:

KBN Engineering and Applied Sciences, Inc.,

Signature:

Date: 6/17/97

APPROVED BY:

Signature:

Date:

STUDY PARAMETERS:

Age or Size of Test Organism:

Valve height, 26-40 mm

Definitive Test Duration:

96 hours

Study Method:

Flow-through

Type of Concentrations:

Mean measured

7. CONCLUSIONS: This study is scientifically sound and fulfills the guideline requirements. A 96-hour EC50 of 68 ppb classifies fluroxypyr 1-methylheptyl ester as highly toxic to the eastern oyster. The NOEC could not be defermined.

#### DATA EVALUATION RECORD § 72-3 - ACUTE EC50 TEST WITH AN ESTUARINE/MARINE MOLLUSK SHELL DEPOSITION STUDY

PC Code No.: 128959 CHEMICAL: Fluroxypyr 1.

Purity: 98.7% 2. TEST MATERIAL: Fluroxypyr

3. CITATION:

R.L. Boeri, P.L. Kowalski, and T.J. Ward Fluroxypyr: Acute Flow-Through Mollusc Authors:

<u>Title:</u>

Shell Deposition Test

February 3, 1994 Study Completion Date:

Laboratory: T.R. Wilbury Laboratories, Inc.,

Marblehead, MA

The Dow Chemical Company, Midland, MI Sponsor:

Laboratory Report ID: 198-DO MRID No.: 440803-11

DP Barcode: D231718

REVIEWED BY: Mark Mossler, M.S., Toxicologist, KBN Engineering and Applied Sciences, Inc.,

Signature: Mullimles Date: 6/17/97

APPROVED BY: Max Feken, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.,

Signature:

My Flu Date: 6/17/97

APPROVED BY: F. Nicholas Mastrota, ERBII, EFED

Signature: J. Nicholas Monstrota Date: 6/30/97

**STUDY PARAMETERS:** 

Valve height, 25-33 mm Age or Size of Test Organism:

Definitive Test Duration: 96 hours

Study Method: Flow-through Type of Concentrations: Mean measured

**CONCLUSIONS:** This study is scientifically sound and fulfills 7. the guideline requirements. A 96-hour EC<sub>50</sub> of 51 ppm classifies fluroxypyr as slightly toxic to the eastern oyster. The NOEC was 16 ppm.

#### ADEQUACY OF THE STUDY:

A. Classification: Core.

B. Rationale: N/A.

C. Repairability: N/A.

9. GUIDELINE DEVIATIONS: None noted.

10. SUBMISSION PURPOSE:

#### 11. MATERIALS AND METHODS:

#### A. Test Organisms

Guideline Criteria	Reported Information
Species Preferred species are the Pacific oyster (Crassostrea gigas) and the Eastern oyster (Crassostrea virginica)	Crassostrea virginica
Mean valve height 25 - 50 mm along the long axis	25 - 33 mm
Supplier	P. Cummins Oyster Co., Pasadena, MD
Are all oysters from same source?	Yes
Are all oysters from the same year class?	Reported as juvenile

#### B. Source/Acclimation

Guideline Criteria	Reported Information
Acclimation Period Minimum 10 days after collection	Acclimated for 13 days prior to testing
Wild caught organisms were quarantined for 7 days?	N/A
Were there signs of disease or injury?	No
If treated for disease, was there no sign of the disease remaining during the 48 hours prior to testing?	N/A

Guideline Criteria	Reported Information
Amount of peripheral shell growth removed prior to testing	2-3 mm
Feeding during the acclimation Must be fed to avoid stress.	Live marine phytoplankton added to unfiltered seawater
Pretest Mortality <3% mortality 48 hours prior to testing	No mortality during the 48 hours prior to testing

## C. Test System

Guideline Criteria	Reported Information
Source of dilution water Natural unfiltered seawater from an uncontaminated source	Unfiltered, aerated seawater collected from the Atlantic Ocean
Does water support test animals without observable signs of stress?	Yes
Salinity 30-34 % salinity, weekly range < 6 %	34-35 %
Water Temperature 15-30° C, consistent in all test vessels	20.0-22.4°C
Hq	7.8-8.3
<u>Dissolved Oxygen</u> ≥ 60% throughout	≥89% of saturation throughout the test
Total Organic Carbon	Not reported
<u>Test Aquaria</u> Should be constructed of glass or stainless steel	Glass aquaria were 20-L in volume containing 15 L of dilution water
Type of Dilution System Must provide reproducible supply of toxicant	Intermittent-flow proportional diluter
Flow rate Consistent flow rate	8.8 volume replacements/24 hr

Guideline Criteria	Reported Information
Was the loading of organism such that each individual sits on the bottom with water flowing freely around it?	Yes
<u>Photoperiod</u> 16 hours light, 8 hours dark	16 hours light, 8 hours dark
Solvents Not to exceed 0.5 ml/L	Solvent: none Maximum conc.: N/A

### D. Test Design

Guideline Criteria	Reported Information
Range Finding Test If EC <sub>50</sub> >100 mg/L with 30 oysters, then no definitive test is required	No preliminary tests were conducted.
Nominal Concentrations of Definitive Test Control & 5 treatment levels; each conc. should be 60% of the next highest conc.; concentrations should be in a geometric series	Control, 16, 28, 44, 66, and 110 mg/L, corrected for purity
Number of Test Organisms Minimum 20 individual per test level and in each control	20 oysters per treatment or control group
Test organisms randomly or impartially assigned to test vessels?	Yes
Biological observations made every 24 hours?	Yes
Water Parameter Measurements  1. Temperature    Measured hourly in at least one chamber  2. DO and pH    Measured at beginning of test—and every 48 h in the high, medium, and low doses and in the control	Temperature was measured continuously in one vessel and daily in each chamber.  DO and pH were measured daily in each chamber.

Guideline Criteria	Reported Information
Was chemical analysis performed to determine the concentration of the test material at the beginning and end of the test? (Optional)	Solutions were collected at initiation, 48 hours after initiation, and at test termination. Samples were filtered and analyzed by HPLC.

#### 12. REPORTED RESULTS:

#### A. General Results

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes
Control Mortality Not more than 10% of control organisms may die or show abnormal behavior	0%·
Control Shell Deposition Must be at least 2 mm	3.0 mm
Recovery of Chemical	93-109% of nominal
Raw data included?	Yes
Signs of toxicity (if any) were described?	Yes

#### Shell Growth

1 *************************************	tration om)	Number Per	Number	Mean Shell Deposition	Mean Percent	
Nominal	Mean Measured	Level	Dead	(mm)	Decrease	
Control	<1.0	20	0	3.0		
16	16	20	0	2.8	7	
28	26	20	0	2.2	27	
44	45	20	0	2.0	33	
66	66	20	0	0.9	70	
110	120	20	0	0.4	. 87	

Other Significant Results: No sublethal effects were noted in the control or treatment groups.

#### B. Statistical Results

Statistical method: Bonferroni's T-test for NOEC determination, weighted least-squares non-linear regression for the EC<sub>50</sub> value

96-hr EC<sub>50</sub>: 51 ppm Probit Slope: N/A 95% C.I.: 42 - 62 ppm

NOEC: 16 ppm

#### 13. VERIFICATION OF STATISTICAL RESULTS:

Parameter	Result
Statistical Method for EC50	non-linear regression
EC <sub>50</sub> (95% C.I.)	51 ppm (42 - 62 ppm)
Probit Slope	N/A 2.35 F.M.M.
Statistical Method for NOEC	Williams' Test
NOEC	16 ppm

14. <u>REVIEWER'S COMMENTS</u>: This study is scientifically sound and can be classified as **Core**. The 96-hour EC<sub>50</sub> for oyster shell deposition was determined to be 51 ppm, which classifies the test material as slightly toxic to the eastern oyster.

File: oys T

Transform: NO TRANSFORMATION

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	Control	20	2.965	2.965	2.965
2	16 ppm	20	2.855	2.855	2.855
3	26 ppm	20	2.175	2.175	2.175
4	45 ppm	20	1.970	1.970	1.970
5	mqq 66	20	0.935	0.935	0.935
6	120 ppm	20	0.455	0.455	0.455

Oyster shell depo. File: oys Ti Transform: NO TRANSFORMATION

WILLIAMS TEST	(Isotonic	regression	model)	TABLE 2 C	0F 2
IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
Control 16 ppm 26 ppm 45 ppm 66 ppm 120 ppm	2.965 2.855 2.175 1.970 0.935 0.455	0.555 3.987 5.022 10.246 12.669	* * *	1.67 1.75 1.77 1.78 1.79	k= 1, v=114 k= 2, v=114 k= 3, v=114 k= 4, v=114 k= 5, v=114

0.627

lote: df used for table values are approximate when v > 20.

NOEC = 16 pm

File:A:oyster.out	Page 1	CONC	shell depo.	REP	15:00 Tuesday,	June 3, 1997	File:A:oyster.out	Page 2 66 67 68	45 45 45	1.65321 1.65321 1.65321	1 1	1.5 1.8 2.0			ÿ.,
	1			1	•					shell depo.		15:00 Tueso	day, June i	3, 1997	٠,
	2	0 0 0	•	1	3.8 2.7 2.9			OBS	CONC	LOG_CONC	REP	Y	·		
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	9	0	•	1	3.1 3.7 3.2			74 75	45 45	1.65321	2	2.4 1.4 2.0			
	11 12	Ö	•	2	4.1 3.4			76 77	45 45	1.65321	2	2.0 2.8 1.6	••		
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	24 25	16 16	1.20412 1.20412 1.20412	1	2.6 2.7			89 90	66 66	1.81954 1.81954	1	0.5 1.3			
	26 27	16 16	1.20412 1.20412	1	3.4			91 92	66 66	1.81954 1.81954	2	1.5 0.0			
	28 29	16 16	1.20412	1	2.5			93 94 05	66 66	1.81954 1.81954 1.81954	5.	0.0 1.5 2.2 1.9		*	
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	37 38	16 16	1.20412	2	2.7 4.5		·	102 103 104	120 120 120	1.81954 1.81954 1.81954 1.81954 1.81954 1.81954 1.81954 1.81954 1.81954 1.81954 1.81954 1.81954 1.81954 1.81954 2.07918 2.07918 2.07918	1	0.7 0.9			
	39 40 41	16 16 16 26 26 26 26 26 26 26 26 26 26	1.20412 1.20412 1.20412 1.41497	2	4.5 2.9 3.0 1.9			105 106	120 120	2.07918 2.07918 2.07918	į	0.9 0.0 1.3			•
	42 43	26 26	1.41497 1.41497 1.41497	i	2.6 1.9 3.7			107 108	120 120	2.07918 2.07918 2.07918	1	0.0 0.0			
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	48 49	26 26	1.41497 1.41497 1.41497	1	2.4 1.8			112 113 114 115 116 117	120 120	2.07918 2.07918	2	0.7 0.0			
	51 52	26 26	1.41497 1.41497 1.41497	5	1.5 3.6 1.4			116 117	120 120	2.07918 2.07918	2	1.3 0.7			
	53	26. 26	1.41497 1.41497	2	2.1			118 119	120 120	2.07918 2.07918	2	0.0 0.5	ł.		
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		•					•								

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File:A:oyster.out Page 3
                                                                                       lFile:A:oyster.out Page 4
                  1.710026
                                  0.346281
                                                  2.976288
                                                                 34,970562
                                                                                                     CO 2.976287670 0.18270855858 2.6144402231 3.3381351176
                                                  2.976288
                  1.710026
                                  0.346281
                                                                 34.970562
NOTE: Convergence criterion met.
                                                                                                                 Asymptotic Correlation Matrix
                                                      Dependent Variable COUNT
   Non-Linear Least Squares Summary Statistics
                                                                                                                   LOG EC25
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                                     Weighted SS
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                                                                                                LOG EC25
                                                                                                                                   -0.884359047
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       Source
                                                                                                               -0.884359047
                                                                                                   SIGMA
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                                    227.10000000
                                                       75.70000000
                                                                                                                -0.778842239
                                                                                                                                  0.5906815278
       Regression
                                                                                                       CO.
                                                                                            shell depo. 15:00 Tuesday, June 3, 1997
MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
       Residual
                              117
                                     34.97056190
                                                       0.29889369
       Uncorrected Total
                              120
                                    262.07056190
                                                                                                                SUMMARY OF NONLTHEAR REGRESSION
       (Corrected Total)
                              119
                                    115.94509210
                                                                                             OBS
                                                                                                    CONC
                                                                                                             LOG EC25
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       Parameter
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                                                       Confidence Interval
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                                                                                                                                             15:00 Tuesday, June 3, 1997
                                                        Lower
                                                                      Upper
                                                                                            MODEL: YOUNG = CO * PROBNORM ((LOG EC25 - LOG CONC) / SIGMA - 0.67449)
       LOG EC50
                   1.710025582 0.04311324623
                                               1.6246414145
                                                               1.7954097486
                   0.346281347 0.04490251407 0.2573536017 0.4352090915
                                                                                                          Plot of COUNT*LOG CONC.
                                                                                                                                    Symbol used is '0'.
          SIGMA
                   2.976287670 0.18270855858 2.6144402231 3.3381351176
                                                                                                          Plot of PRED*LOG CONC.
                                                                                                                                    Symbol used is '.'.
             CO
                                                                                        COUNT
                         Asymptotic Correlation Matrix
                                                                                         4.5 0
                            LOG_EC50
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                                                                         CO
        Corr
        LOG EC50
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                                                              -0.804685248
                       -0.682380354
                                                              0.5906815278
           SIGMA
                       -0.804685248
                                          0.5906815278
               CO
         shell depo. 15:00 Tuesday, June 3, 1997
MODEL: COUNT = CO * PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
                                                                                          4.0
                        SUMMARY OF NONLINEAR REGRESSION
            CONC
                     LOG_EC50
                                   SIGMA
                                                 CO
                                                          RESID_SS
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     OBS
               O
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                                             2.97629
                                                           34.9706
                                                                      51.2892
                                                                                         3.5
    shell depo. 15:00 Tuesday, June 3, MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
                                                      15:00 Tuesday, June 3, 1997
                               WEIGHTED REGRESSION
                    Non-Linear Least Squares Iterative Phase
                                                                                         3.0 0
                Dependent Variable COUNT Method: Gauss-Newton
                  LOG EC25
                                     SIGMA
                                                               Weighted SS
      Iter
                  1.485000
                                  0.345000
                                                  2.925000
                                                                 37.163321
                                                                                              0
                  1.476468
                                  0.346542
                                                  2.976335
                                                                 34.938174
                                                                                              ñ
                                  0.346281
                                                  2.976287
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                                  0.346281
                                                                 34.970562
NOTE: Convergence criterion met.
                                                                                                                                0
   Non-Linear Least Squares Summary Statistics
                                                      Dependent Variable COUNT
                                                                                              -0
                                                                                                              0
                                                                                          2.0
                                     Weighted SS
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       Source
                                                                                                              0
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                                    227.10000000
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       Regression
                              117
                                     34,97056190
                                                       0.29889369
       Residual
                              120
                                    262.07056190
       Uncorrected Total
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       (Corrected Total)
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                                    115.94509210
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                      Estimate
                                   Asymptotic
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       Parameter
                                   Std. Error
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                   1.476462276 0.06751322234
                                                1.3427548715 1.6101696806
                                                                                          1.0
       LOG EC25
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                                                                                                                                                                Ö
                   0.346281347 0.04490251407 0.2573536017 0.4352090915
                                                                                                                                           0
          SIGMA
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NOTE: 916 obs had missing values. 929 obs hidden. shell depo. 15:

shell depo. 15:00 Tuesday, June 3, 1997
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL

General Linear Models Procedure Class Level Information

Class Levels Values

DOSE 6 0 16 26 45 66 120

Number of observations in data set = 120

shell depo. 15:00 Tuesday, June 3, 1997
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL

#### General Linear Models Procedure

Dependent V	ariable:	RESPONSE				
Source		DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	•	5	102.9137500	20.5827500	52.43	0.0001
Error		114	44.7495000	0.3925395		
Corrected T	otal	119	147.6632500			
	R	-Square	c.v.	Root MSE	RESP	ONSE Mean
	0	.696949	33.10593	0.626530		1.892500
Source		DF	Type I SS	Mean Square	F Value	Pr > F
DOSE		5	102.9137500	20.5827500	52.43	0.0001
Source		DF	Type III SS	Mean Square	F Value	Pr > F
DOSE		5	102.9137500	20.5827500	52.43	0.0001

shell depo. 15:00 Tuesday, June 3, 1997
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL

General Linear Models Procedure

|File:A:oyster.out Page 6

Level o	f	RESP	ONSE		
DOSE	N	Mean	SD		
0	20	2.96500000	0.60981015		
16	20	2.85500000	0.58081159		
26	20	2.17500000	0.75594138		
26 45	20	1.97000000	0.52224213		
66	20	0.93500000	0.74146015		
120	20	0.45500000	0.50207464		
		shell depo.	15:00 Tuesday,	June 3,	1997
COMPAR	RISON OF	MEANS FOR NOEL	DETERMINATION		
TEST	T IF TREA	THENT IS LESS T	HAN CONTROL .		

#### General Linear Models Procedure

Dunnett's One-tailed T tests for variable: RESPONSE

NOTE: This tests controls the type I experimentwise error for comparisons of all treatments against a control.

Alpha= 0.05 Confidence= 0.95 df= 114 MSE= 0.392539 Critical Value of Dunnett's T= 2.260 Minimum Significant Difference= 0.4477

Comparisons significant at the 0.05 level are indicated by '\*\*\*'.

DOSE Comparison	Simultaneous Lower Confidence Limit	Difference Between Means	Simultaneous Upper Confidence Limit	
16 - 0	-0.5577	-0.1100	0.3377 -0.3423	***
26 - 0 45 - 0	-1.2377 -1.4427	-0.7900 -0.9950	-0.5473	***
66 - 0 120 - 0	-2.4777 -2.9577	-2.0300 -2.5100	-1.5823 -2.0623	***

#### DATA EVALUATION RECORD § 72-3 - ACUTE LC. TEST WITH AN ESTUARINE/MARINE SHRIMP

PC Code No.: 128959 1. CHEMICAL: Fluroxypyr

Purity: 98.7% 2. TEST MATERIAL: Fluroxypyr

3. CITATION:

> Authors: R.L. Boeri, P.L. Kowalski, and T.J. Ward

Fluroxypyr: Acute Toxicity to the Grass Title:

Shrimp, Palaemonetes pugio

February 14, 1994 Study Completion Date:

T.R. Wilbury Laboratories, Inc., Laboratory:

Marblehead, MA

The Dow Chemical Company, Midland, MI Sponsor:

Laboratory Report ID: 197-DO

MRID No.: 440803-12 DP Barcode: D231718

REVIEWED BY: Mark Mossler, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.,

Signature: Mit Shouls

Date: 6/17/97

APPROVED BY: Max Feken, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.,

Signature:

W flu Date: 6/17/97 APPROVED BY: F. Nicholas Mastrota, ERBIT, EFED

signature: J. Nicholas Mastrota Date: 7/2/97

6. STUDY PARAMETERS:

Age or Size of Test Organism:

Juvenile

Definitive Test Duration: 96 hours Study Method: Flow-through

Type of Concentrations: Mean measured

7. **CONCLUSIONS:** This study is scientifically sound and fulfills the guideline requirements. The 96-hour LC50 for grass shrimp was determined to be >120 ppm, which classifies fluroxypyr as practically non-toxic to the grass shrimp.

#### Results Synopsis:

 $LC_{50}$ : >120 ppm

95% C.I.: N/A

NOEC: 120 ppm

Probit Slope: N/A

#### 8. ADEQUACY OF THE STUDY:

A. Classification: Core

B. Rationale: N/A

C. Repairability: N/A

9. GUIDELINE DEVIATIONS: None noted.

10. SUBMISSION PURPOSE:

#### 11. MATERIALS AND METHODS:

#### A. Test Organism

Guideline Criteria	Reported Information
<u>Species</u> Preferred species are Mysidopsis bahia, Penaeus setiferus, P. duorarum, P. aztecus and Palaemonetes sp.	Palaemonetes pugio
<pre>Age Juvenile, mysids should be ≤24 hours old</pre>	Reported to be juveniles, average wet weight and length of control shrimp at the end of the test were 0.18 g and 26 mm, respectively
Supplier	Multi Aquaculture Systems, Amagansett, NY
All shrimp from same source?	Yes
All shrimp from the same year class?	Yes

#### B. Source/Acclimation

Guideline Criteria	Reported Information
Acclimation Period Minimum 10 days	Held under test conditions for 14 days prior to testing
Wild caught organisms were quarantined for 7 days?	N/A
Were there signs of disease or injury?	No

Guideline Criteria	Reported Information
If treated for disease, was there no sign of the disease remaining during the 48 hours prior to testing?	N/A
Feeding No feeding during the study and no feeding for 24 hours before the beginning of the test if organisms are over 0.5 g each	Not fed during testing
Pretest Mortality <3% mortality 48 hours prior to testing	Less than 3% mortality during the last 48 hours of acclimation

## C. Test System

Guideline Criteria	Reported Information
Source of dilution water Soft reconstituted water or water from a natural source, not dechlorinated tap water	Seawater was collected from the Atlantic Ocean and the salinity adjusted to 11-17 parts per thousand. The water was aerated, carbon-filtered, filtered, and UV sterilized.
Does water support test animals without observable signs of stress?	Yes
<pre>Salinity 30-34 % for marine (steno- haline) shrimp, 10-17 % for estuarine (euryhaline) shrimp, weekly range &lt;6 %</pre>	16-17 ‰
<u>Water Temperature</u> 22 <u>+</u> 1 °C	21.8-22.7°C
<pre>pH 8.0-8.3 for marine (steno- haline) shrimp, 7.7-8.0 for estuarine (euryhaline) shrimp, monthly range &lt; 0.8</pre>	7.5-7.9

a : , , ;	Described Tables tion
Guideline Criteria	Reported Information
Dissolved Oxygen Static: ≥ 60% during 1st 48 hrs and ≥ 40% during 2nd 48 hrs, flow-through: ≥ 60%	≥75% saturation
Test Aquaria  1. Material: Glass or stainless steel  2. Size: 19.6 L is acceptable for organisms ≥0.5 g (e.g. pink, white, and brown shrimp), 3.9 L is acceptable for smaller organisms (e.g. mysid or grass shrimp)  3. Fill volume: 15 L is acceptable for organisms ≥0.5 g, 2-3 L is acceptable for smaller organisms	Glass 10-L 7.5 L
Type of Dilution System Must provide reproducible supply of toxicant	of $st_{\infty}k$ solution Continuous flow, no dilution needed
Flow Rate Consistent flow rate of 5-10 vol/24 hours, meter systems calibrated before study and checked twice daily during test period	5.8 volume replacements/24 hr
Biomass Loading Rate Static: ≤ 0.8 g/L at ≤ 17°C, ≤ 0.5 g/L at > 17°C; flow- through: ≤ 1 g/L/day	0.06 g/L/day
<pre>Photoperiod 16 hours light, 8 hours dark</pre>	16 h light, 8 h dark
<pre>Solvents Not to exceed 0.5 mL/L for static tests or 0.1 mL/L for flow-through tests</pre>	Solvent: none Maximum conc.: N/A

### D. Test Design

Guideline Criteria	Reported Information
Range Finding Test  If LC <sub>50</sub> >100 mg/L with 30 shrimp, then no definitive test is required.	No mortality after 96 hours of exposure at concentrations of up to 100 ppm
Nominal Concentrations of Definitive Test Control & 5 treatment levels; dosage should be 60% of the next highest concentration; concentrations should be in a geometric series	Control and 120 mg/L, corrected for purity
Number of Test Organisms Minimum 10/level, may be di- vided among containers	30 shrimp per treatment or control group, 15 per replicate vessel
Test organisms randomly or impartially assigned to test vessels?	Yes
Biological observations made every 24 hours?	Yes
<pre>Water Parameter Measurements 1. Temperature    Measured constantly or, if    water baths are used, every    6 hrs, may not vary &gt; 1°C 2. DO and pH    Measured at beginning of    test and ever 48 h in the    high, medium, and low doses    and in the control</pre>	Temperature measured at least every 6 hours in one test chamber and daily in each chamber  DO and pH measured daily in each chamber
Chemical Analysis Needed if solutions were aerated, if chemical was volatile, insoluble, or known to absorb, if precipitate formed, if containers were not steel or glass, or if flow- through system was used	Solutions were collected from both groups at test initiation, 48 hours after initiation, and termination. The solutions were filtered and analyzed by HPLC.

## 12. REPORTED RESULTS:

#### A. General Results

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes
Recovery of Chemical	100%
Control Mortality Not more than 10% control organisms may die or show abnormal behavior.	3.3%
Raw data included?	Yes
Signs of toxicity (if any) were described?	Yes

# **Mortality**

Concentrati Nominal	on (ppm)  Mean Measured	Number of Shrimp	Cum	ulative Hour o	Number I f Study 72	Dead 96
Control	<1.0	30	0	0	1	1
120	120	30	0	0	0	0

Other Significant Results: No sublethal effects were noted.

B. Statistical Results: No statistical analyses were conducted.

96-hr LC<sub>50</sub>: >120 ppm 95% C.I.: N/A Probit Slope: N/A NOEC: 120 ppm 13. VERIFICATION OF STATISTICAL RESULTS:

Parameter	Result
Binomial Test LC <sub>50</sub> (C.I.)	N/A
Moving Average Angle LC <sub>50</sub> (95% C.I.)	N/A
Probit LC <sub>50</sub> (95% C.I.)	N/A
Probit Slope	N/A
NOEC	120 ppm

14. REVIEWER'S COMMENTS: This study is scientifically sound, fulfills the guideline requirements for an acute toxicity study, and can be classified as Core. The 96-hour LC<sub>50</sub> value of >120 ppm classifies fluroxypyr as practically non-toxic to the grass shrimp.

# DATA EVALUATION RECORD § 72-3 - ACUTE LCs TEST WITH AN ESTUARINE/MARINE SHRIMP

128968

PC Code No.: 128959 CHEMICAL: Fluroxypyr

TEST MATERIAL: Fluroxypyr 1-methylheptyl ester Purity: 95.8% 2.

CITATION: 3.

> R.L. Boeri, P.L. Kowalski, and T.J. Ward Authors:

Fluroxypyr 1-Methylheptyl Ester: Acute Title:

Toxicity to the Grass Shrimp,

Palaemonetes pugio

Study Completion Date: December 7, 1995

T.R. Wilbury Laboratories, Inc., Laboratory:

Marblehead, MA

The Dow Chemical Company, Midland, MI Sponsor:

<u>Laboratory Report ID:</u> 706-DO

MRID\_No.: 440803-13 DP Barcode: D231718

Mark Mossler, M.S., Toxicologist, REVIEWED BY:

KBN Engineering and Applied Sciences, Inc.,

Date: 6/17/97

APPROVED BY: Max Feken, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.,

Signature:

My John

Date: 6/17/97

APPROVED BY: F. Nicholas Mastrota, ERBII, EFED

Signature: F. Nicholas Mastrota ··Date:

**STUDY PARAMETERS:** 

Age or Size of Test Organism: Juvenile

Definitive Test Duration: 96 hours

Study Method: Flow-through

Type of Concentrations: Mean measured

**CONCLUSIONS:** This study is scientifically sound and fulfills the guideline requirements. The 96-hour LC50 was determined to be >0.135 ppm (>100 ppm nominal), which classifies the 1methylheptyl ester of fluroxypyr as practically non-toxic to the grass shrimp (i.e., it is not toxic at its solubility limit).

Results Synopsis:

LC<sub>50</sub>: >0.135 ppm (>100 ppm nominal) 95% C.I.:

NOEC: 0.135 ppm (100 ppm nominal) Probit Slope: N/A

# 8. ADEQUACY OF THE STUDY:

A. Classification: Core

B. Rationale: N/A

C. Repairability: N/A

9. GUIDELINE DEVIATIONS: None noted.

# 10. SUBMISSION PURPOSE:

# 11. MATERIALS AND METHODS:

# A. Test Organism

Guideline Criteria	Reported Information
Species Preferred species are Mysidopsis bahia, Penaeus setiferus, P. duorarum, P. aztecus and Palaemonetes sp.	Palaemonetes pugio
<u>Age</u> Juvenile, mysids should be ≤24 hours old	Reported to be juveniles, average wet weight and length of control shrimp at the end of the test were 0.084 g and 29 mm, respectively
Supplier	Aquatic Research Organisms, Hampton, NH
All shrimp from same source?	Yes
All shrimp from the same year class?	Not specified

# B. Source/Acclimation

Guideline Criteria	Reported Information
Acclimation Period Minimum 10 days	Held under test conditions for 14 days prior to testing
Wild caught organisms were quarantined for 7 days?	N/A
Were there signs of disease or injury?	No

Guideline Criteria	Reported Information
If treated for disease, was there no sign of the disease remaining during the 48 hours prior to testing?	N/A
Feeding No feeding during the study and no feeding for 24 hours before the beginning of the test if organisms are over 0.5 g each	Not fed 48 hours prior to or during testing
<pre>Pretest Mortality &lt;3% mortality 48 hours prior to testing</pre>	No mortality during the last 48 hours of acclimation

# C. Test System

Guideline Criteria	Reported Information
Source of dilution water Soft reconstituted water or water from a natural source, not dechlorinated tap water	Seawater was collected from the Atlantic Ocean and the salinity adjusted to 11-17 parts per thousand. The water was aerated, carbon-filtered, filtered, and UV sterilized.
Does water support test animals without observable signs of stress?	Yes
<pre>Salinity 30-34 % for marine (steno- haline) shrimp, 10-17 % for estuarine (euryhaline) shrimp, weekly range &lt;6 %</pre>	15-17 ‰
Water Temperature 22 ± 1 °C	22.0-22.8°C
<pre>pH 8.0-8.3 for marine (steno- haline) shrimp, 7.7-8.0 for estuarine (euryhaline) shrimp, monthly range &lt; 0.8</pre>	7.4-7.8

Guideline Criteria	Reported Information
<pre>Dissolved Oxygen Static: ≥ 60% during 1st 48 hrs and ≥ 40% during 2nd 48 hrs, flow-through: ≥ 60%</pre>	≥75% saturation
Test Aquaria 1. Material: Glass or stainless steel 2. Size: 19.6 L is acceptable for organisms ≥0.5 g (e.g. pink, white, and brown	Glass 20-L
shrimp), 3.9 L is acceptable for smaller organisms (e.g. mysid or grass shrimp)  3. Fill volume: 15 L is acceptable for organisms >0.5 g, 2-3 L is acceptable for smaller organisms	15 L
Type of Dilution System Must provide reproducible supply of toxicant	Intermittent-flow diluter
Flow Rate Consistent flow rate of 5-10 vol/24 hours, meter systems calibrated before study and checked twice daily during test period	6.7 volume replacements/24 hr
Biomass Loading Rate Static: ≤ 0.8 g/L at ≤ 17°C, ≤ 0.5 g/L at > 17°C; flow- through: ≤ 1 g/L/day	0.013 g/L/day
<u>Photoperiod</u> 16 hours light, 8 hours dark	16 h light, 8 h dark
<pre>Solvents Not to exceed 0.5 mL/L for static tests or 0.1 mL/L for flow-through tests</pre>	Solvent: DMF Maximum conc.: 0.5 mL/L

# D. Test Design

Guideline Criteria	Reported Information
Range Finding Test  If LC <sub>50</sub> >100 mg/L with 30 shrimp, then no definitive test is required.	No mortality after 96 hours of exposure at concentrations of 0.01, 0.1, 1, and 10 ppm. Insoluble material was noted at the 1 and 10 ppm levels.
Nominal Concentrations of Definitive Test Control & 5 treatment levels; dosage should be 60% of the next highest concentration; concentrations should be in a geometric series	Control and 100 mg/L, corrected for purity
Number of Test Organisms Minimum 10/level, may be di- vided among containers	30 shrimp per treatment or control group, 15 per replicate vessel
Test organisms randomly or impartially assigned to test vessels?	Yes
Biological observations made every 24 hours?	Yes
<pre>Water Parameter Measurements 1. Temperature    Measured constantly or, if    water baths are used, every    6 hrs, may not vary &gt; 1°C 2. DO and pH    Measured at beginning of    test and ever 48 h in the    high, medium, and low doses    and in the control</pre>	Temperature measured at least every 6 hours in one test chamber and daily in each chamber  DO and pH measured daily in each chamber
Chemical Analysis Needed if solutions were aerated, if chemical was volatile, insoluble, or known to absorb, if precipitate formed, if containers were not steel or glass, or if flow- through system was used	Replicate solutions were collected at test initiation, 48 hours after initiation, and termination. Half of the samples were filtered and analyzed by HPLC. The other half were stored as backup samples.

#### 12. REPORTED RESULTS:

#### A. General Results

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes
Recovery of Chemical	<1% of nominal
Control Mortality Not more than 10% control organisms may die or show abnormal behavior.	No mortality in the control group
Raw data included?	Yes
Signs of toxicity (if any) were described?	Yes

#### Mortality

Concentrat  Nominal	ion (ppm)  Mean Measured	Number of Shrimp	Cun 24	Hour of		Dead 96
Control	<0.063	30	0	О	0	0
100	0.135	30	0	0	0	, 0

Other Significant Results: Particulate matter was observed in the treatment solution.

#### B. Statistical Results

Method: Visual interpretation

96-hr LC<sub>50</sub>: >0.135 ppm 95% C.I.: N/A Probit Slope: N/A NOEC: 0.135 ppm

- precluded the use of regression analysis to determine the LC<sub>50</sub>. It is apparent that the 96-hour LC<sub>50</sub> is greater than the maximum saltwater solubility of the test material.
- 14. REVIEWER'S COMMENTS: The test material was supplied to the aquaria at a concentration of 100 ppm. However, the test

material was reported to be soluble in water only to a concentration of 100 ppb (at 25°C). The authors used solvent (DMF; 0.5 mL/L) and a high shear pump to mix the treatment solution. It is therefore apparent that every effort was made to solubilize the test material in saltwater. Consequently, this study is scientifically sound and can be classified as Core. The 96-hour LC50 for grass shrimp was determined to be >100 ppm (>0.135 ppm mean measured), which classifies the test material as practically non-toxic to the grass shrimp. The NOEC was 100 ppm (0.135 ppm mean measured).

TINIU NO. 440803-3

# DATA EVALUATION RECORD ALGAE OR DIATOM EC<sub>50</sub> TEST GUIDELINE 123-2 (TIER II)

128968 J.M.

1. <u>CHEMICAL</u>: Fluroxypyr

Do 128968 J.M.

PC Code No.: 128959

6/26/97

2. TEST MATERIAL: Fluroxypyr 1-methylheptyl ester Purity: 95.8%

3. CITATION:

Authors: D.P. Milazzo, A.M. Landre, J.M. Hugo, and

M.D. Martin

Title: Fluroxypyr 1-Methylheptyl Ester: The

Toxicity to the Freshwater Diatom,

Navicula pelliculosa

Study Completion Date: June 4, 1996

Laboratory: Environmental Toxicology & Chemistry

Research Laboratory, The Dow Chemical

Company, Midland, MI

Sponsor: DowElanco, Indianapolis, IN

<u>Laboratory Report ID</u>: ES-3075

DP Barcode: D231718
MRID No.: 440803-39

4. REVIEWED BY: Mark A. Mossler, M.S., Toxicologist,

KBN Engineering and Applied Sciences, Inc.

Signature: Mark Marken

Date: 6/17/97

APPROVED BY: Pim Kosalwat, Ph.D., Senior Scientist,

KBN Engineering and Applied Sciences, Inc.

Bignature: P. Kosalwat

Date: 6/17/97

5. APPROVED BY: F. Nicholas Mastroto, Wildlife Biologist, ERBII, EFED

signature: I Nicholas Mastrota Date: 6/26/97

6. STUDY PARAMETERS:

Definitive Test Duration: 120 hours

Type of Concentrations: Initial measured

7. <u>CONCLUSIONS</u>: This study is not scientifically sound and does not fulfill the guideline requirements for an algal toxicity test.

8. ADEQUACY OF THE STUDY:

A. Classification: Invalid.

- B. Rationale: The solvent control solutions were contaminated with test material. Negative control data were not included in the report.
- C. Repairability: Yes; if the negative control data exists, and was inadvertently omitted, the treatment data can be reanalyzed in comparison with the negative control data.

## 9. GUIDELINE DEVIATIONS:

- 1. The concentration of solvent in the solvent control and treatment solutions was not specified.
- 2. The solvent control solutions were contaminated with test material.
- 3. Negative control data were not reported.

## 10. SUBMISSION PURPOSE:

#### 11. MATERIALS AND METHODS:

#### A. Test Organisms

Guideline Criteria	Reported Information
<u>Species</u> Skeletonema costatum Anabaena flos-aquae Selenastrum capricornutum Navicula pelliculosa	Navicula pelliculosa
Initial Number of Cells 3,000 - 10,000 cells/mL	10,000 cells/mL
<u>Nutrients</u> Standard formula, e.g. 20XAAP	Algal assay medium with silicon and selenium

## B. Test System

Guideline Criteria	Reported Information
<u>Solvent</u>	Acetone
Temperature Skeletonema: 20°C Others: 24-25°C	24.4-25.9°C

TAXID NO. 440003-33

Guideline Criteria	Reported Information
Light Intensity Anabaena: 2.0 KLux (±15%) Others: 4.0-5.0 KLux (±15%)	3.2-5.4 KLux
Photoperiod Skeletonema: 14 h light, 10 h dark or 16 h light, 8 h dark Others: Continuous	Continuous
<u>pH</u> Skeletonema: approx. 8.0 Others: approx. 7.5	7.4-8.1

# C. Test Design

Guideline Criteria	Reported Information
Dose range 2X or 3X progression	16, 31, 63, 125, 250, and 500 ppb
<u>Doses</u> at least 5	6
<pre>Controls negative and/or solvent</pre>	Solvent (acetone) control
Replicates per dose 3 or more	4
<u>Duration of test</u> 120 hours	120 hours
Daily observations were made?	Counts on days 3, 4, and 5
Method of Observations	Cellular counts
Maximum Labeled Rate	0.25 lb acid equivalents/acre

# 12. REPORTED RESULTS:

Guideline Criteria	Reported Information
Initial and 120 h cell densities were measured?	Yes
Control cell count at 120 hr ≥2X initial count?	Yes

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Guideline Criteria	Reported Information
Initial chemical concentrations measured? (Optional)	Yes
Raw data included?	Yes

#### Dose Response

Initial measured concentration (µg/L)	Avg. Cell Density (x 10° cells/mL)	% Inhibition*
Solvent Control	64.2	-
15	55.9	13
33	51.0	21
75	46.7	27
132	38.4	40
217	2.6	96
.500	0.5	99

<sup>\*</sup>Inhibition was based upon comparison to the solvent control.

Other Significant Results: The solvent control solutions were contaminated with the test material at a concentration of approximately 21 ppb.

## Statistical Results for Cell Density:

Statistical Method: Least squares linear regression analysis and analysis of variance coupled with Dunnett's test

EC<sub>50</sub>: 93 ppb

95% C.I.: 13-640 ppb

Probit Slope: N/A

NOEC: 132 ppb

- 13. <u>VERIFICATION OF STATISTICAL RESULTS</u>: No statistical analyses were conducted due to the invalidity of the results.
- 14. REVIEWER'S COMMENTS: In the methods section of the report, it was stated that a negative control and a solvent control group were prepared at test initiation. In the analytical section of the report, the results presented indicated that there was a negative control group which was analyzed in conjunction with the solvent control group. The results of

CTODORF FOR GENERAL

the analyses indicated that the negative control solutions were uncontaminated and the solvent control solutions were contaminated with test material. Ideally, the negative control group could serve as the control group used for comparison in this test since the solvent control group solutions were contaminated. However, the raw data and means of the negative control group were not presented in the report. The reviewer questions why these data were omitted, since the other four aquatic plant reports with the test material contain the raw and mean data for the negative control group. Consequently, this study is not scientifically sound and does not fulfill the guideline requirements for an algal toxicity test. This study is categorized as Invalid.

308/2E August 8,1997



Document Processing Desk Office of Pesticide Programs (7504C) U.S. Environmental Protection Agency Room 266A, Crystal Mall 2 1921 Jefferson Davis Highway Arlington, VA 22202

Attention: Joanne I. Miller/PM-23 (7505C)

FLUROXYPYR: PP#6F4772

EPA FILE SYMBOL NUMBER: STARANE\* F (62719-EIL)
EPA FILE SYMBOL NUMBER: STARANE EC (62719-EIA)

REVISION TO DATA FORMAT DEFICIENCY ON SUBMISSION DATED AUGUST 6, 1996

Enclosed please find three copies of a revised page 4 (Quality Assurance Statement) for study number K-137992-013. A copy of this revised page was faxed directly to Linda Taylor at the EPA August 7, 1997 per her earlier request. The study initiation date and the data and draft report audit dates on the original page were incorrect.

This study was originally submitted August 6, 1996 on the Application for New Registration - Section 3, with the Petition for Permanent Tolerance for Fluroxypyr Methylheptyl Ester (MHE) Residues on Wheat, Barley and Oats. The assigned MRID is 44080319.

#### Contents of Submission

Correction	Volume No.	Stud	<u>iv</u>
Revised Page Page	Volume 19	Fluroxypyr Methylheptyl Ester	: Oral Gavage Teratology
4R	83-3(b)	Study in New Zealand White R	abbits
		Liberacki, A.B.	May 2, 1996
		Study ID: K-137992-013	(3 copies)

If you require further information, please contact me at the number listed below or Joyce Armstrong, Registration Assistant for this product, at (317) 337-4657.

Sincerely,

Robert F. Bischoff
Regulatory Manager
U.S. Regulatory, Toxicology and
Environmental Chemistry
(317) 337-4686

(317) 337-4649 (FAX)

RFB/jla/caa Enclosures

Trademark of DowElanco

# QUALITY ASSURANCE STATEMENT

Compound: FLUROXYPYR METHYLHEPTYL ESTER

Title: FLUROXYPYR METHYLHEPTYL ESTER: ORAL GAVAGE

TERATOLOGY STUDY IN NEW ZEALAND WHITE RABBITS

This study was examined for conformance with Good Laboratory Practices as published by the U.S. Environmental Protection Agency. The final report was determined to be an accurate reflection of the data obtained. The dates of Quality Assurance activities on this study are listed below.

Study Initiation Date: 31 July 1995

TYPE OF AUDIT:	DATE OF AUDIT:	DATE FINDINGS REPORTED TO STUDY DIRECTOR/MANAGEMENT:
Preliminary protocol	28 July 1995	28 July 1995
Final protocol	10 August 1995	10 August 1995
Protocol, study conduct	31 August 1995	31 August 1995
Data, and draft report	20-25 March 1996	25 March 1996
Final Report	1 May 1996	1 May 1996
Report change/revision 1	29 July 1996	29 July 1996
Report change/revision 2	18 June 1997	18 June 1997

K. T. Haut, B. S.

(Date)

Quality Assurance

Health and Environmental Research Laboratories

The Dow Chemical Company

1803 Building

Midland, Michigan 48674

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Quality Assurance

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STUDY ID: K-137992-013

PAGE 4R

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K. T. Haut, B. S.

(Date)

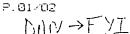
Quality Assurance

Health and Environmental Research Laboratories

The Dow Chemical Company

1803 Building

Midland, Michigan 48674



Toan



# Platte Chemical Co.

. 419 18th Street (80631-5852) P.O. Box 667 Greeley, CO 80632-0667

Fax 970-356-4418

Ph. 970-356-4400

changed rankin.  $o \in$ 

March 17, 1997

Dr. Peter Caulkins, Deputy Director Registration Division (7505C) Office of Pesticide Programs U.S. Environmental Protection Agency 401 M Street, S.W. Washington, D.C. 20460-0001

Subject:

Fluroxypyr-MHE Priority Change from EUP to Section 3

Dear Sir:

As requested, following our discussion of March 14, 1997, Platte Chemical Co. (Platte) formally requests in writing that your office change Platte's priority item (as was originally requested in November 17, 1995) from an EUP for a temporary tolerance for Fluroxypyr on small grains to a Section 3 registration for Fluroxypyr on small grains.

As previously described, Platte formed a business arrangement with DowElanco to register fluroxypyr for the small grains herbicide market. Platte has shouldered all registration data generation costs since that business arrangement was formed in 1995 and will continue to do so. Platte has made and will continue to make significant financial and administrative investments for the registration and maintenance of fluroxypyr.

Please note that Platte has, to date, only requested 2 priorities.

The complete submission for fluroxypyr (also referred to as Starane EC) for use on wheat, barley, and oats was made on August 11, 1996. EPA assigned Starane EC (end use product) the registration number 62719-EIA and Starane F (technical product) the registration number 62719-EIL. The petition number for residue tolerances of fluroxypyr on wheat, barely, and oats is PP 6F4772.



Document Processing Desk Office of Pesticide Programs (7504C) U. S. Environmental Protection Agency Room 266A, Crystal Mall 2 1921 Jefferson Davis Highway Arlington, VA 22202

Attention: Ms. Joanne I. Miller/PM-23 (7505C)

FLUROXYPYR: PP#6F4772

EPA FILE SYMBOL NUMBER: STARANE F (62719-EIL) EPA FILE SYMBOL NUMBER: STARANE EC (62719-EIA)

CONFIRMATION OF PROJECT RELATIONSHIP WITH PLATTE CHEMICAL COMPANY

FOR STARANE\*

Per your request to Bruce Riggle of Platte Chemical, this letter is being faxed to you to confirm that our partner in the above mentioned project for Starane\* products is Platte Chemical Company. They are responsible in the U.S. for the development and commercialization of these new products containing fluroxypyr for use on wheat, barley, and oats and certain other end uses. DowElanco originally submitted a request for new registrations on August 6, 1996 on behalf of Platte Chemical. It is pertinent to note that Platte Chemical has provided significant funding to complete the studies required to support the subject registrations.

If you require further information, please contact me at the number listed below or Ms. Joyce Armstrong, Registration Assistant for this product, at (317) 337-4657.

Sincerely,

Robert F. Bischoff

Product Registration Manager

U.S. Regulatory, Toxicology and Environmental Chemistry

Robert J. Buck off a

(317) 337-4686

(317) 337-4649 (FAX)

RFB/jla

Enclosures

cc: Mr. Bruce Riggle, Platte Chemical Company (United Agri Products)

\*Trademark of DowElanco

Fax RFB 3-10.doc



# UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND **TOXIC SUBSTANCES** 

November 20, 1996

MEMORANDUM:

SUBJECT:

New Chemical Screen for Fluroxypyr. Chemistry and Toxicology Data

Requirements. PC Codes 128959 and 128968. Petition # 6F4772 (Wheat, Barley,

and Oats). DP Barcode: D230602.

FROM:

Catherine Eiden, Chemist

Registration Section

Risk Characterization and Analysis Branch

Health Effects Division (7509C)

THRU:

Deborah L. McCall, Acting Team Leader Registration Section

Registration Section

Risk Characterization and Analysis Branch

Health Effects Division (7509C)

TO:

Dan Kenny, PM-23

Ē Fungicide/Herbicide Branch

Registration Division (7505C)

The following toxicology and residue and product chemistry data, submitted to support a Section 3 registration of the new chemical fluroxypyr for use on wheat, barley, and oats (6F4772) have been screened for completeness and general acceptability for scientific review:

Guideline No.	Toxicology Data	MRID#
81-1	Acute Oral (End-Use Product)	44080329
81-2	· Acute Dermal (End-Use Product)	44080330
81-3	Acute Inhalation (End-Use Product)	44080331
81-4	Primary Eye Irritation (End-Use Product)	44080332



3-1)	Skin Sensitization (End-Use Product)  13-Week Dietary Toxicity Study  18-Month Oncogenic/Dietary Study (mice)  Teratology Study (rat)  Range Finding Study  Teratology Study (rabbits)  Range Finding Study  2-Generation Reproduction (rats)  2-Year Chronic Feeding (rats)  Mutagenicity  Rat Metabolism	44080334 44080316 44080317 44094901 44080318 44080319 44080320 44080321 44080322 44080323 thru 44080324 44080327
	18-Month Oncogenic/Dietary Study (mice) Teratology Study (rat) Range Finding Study Teratology Study (rabbits) Range Finding Study 2-Generation Reproduction (rats) 2-Year Chronic Feeding (rats) Mutagenicity	44080317  44094901  44080318  44080319  44080320  44080321  44080322  44080323  thru  44080324
	Teratology Study (rat) Range Finding Study Teratology Study (rabbits) Range Finding Study 2-Generation Reproduction (rats) 2-Year Chronic Feeding (rats) Mutagenicity	44094901 44080318 44080319 44080320 44080321 44080322 44080323 thru 44080324
	Range Finding Study Teratology Study (rabbits) Range Finding Study 2-Generation Reproduction (rats) 2-Year Chronic Feeding (rats) Mutagenicity	44080318 44080319 44080320 44080321 44080322 44080323 thru 44080324
	Teratology Study (rabbits)  Range Finding Study  2-Generation Reproduction (rats)  2-Year Chronic Feeding (rats)  Mutagenicity	44080319 44080320 44080321 44080322 44080323 thru 44080324
	Range Finding Study  2-Generation Reproduction (rats)  2-Year Chronic Feeding (rats)  Mutagenicity	44080320 44080321 44080322 44080323 thru 44080324
3-1)	2-Generation Reproduction (rats) 2-Year Chronic Feeding (rats) Mutagenicity	44080321 44080322 44080323 thru 44080324
3-1)	2-Year Chronic Feeding (rats)  Mutagenicity	44080322 44080323 thru 44080324
3-1)	Mutagenicity	44080323 thru 44080324
·		thru 44080324
	Rat Metabolism	44080327
	•	
•	Review of Mammalian Toxicology	44080329
ne No.	Product Chemistry Data	MRID #
61	Product Identity and Composition (Technical)/(End Lie Product)	44080301/44080304
52	(Technical)/(End-Use Product) Analysis and Certification of Product	44080302/44080305
	Ingredients (Technical)/(End-Use Product) Physical and Chemical Characteristics (Technical)/(End-Use Product)	44080303/44080306
ne No.	Residue Chemistry	MRID#
)	Nature of Residue (Goats)	44080351
·)	Analytical Method (parent + metabolite) ILV for Analytical Method	44080352 44080353
	)	Nature of Residue (Goats)  Analytical Method (parent + metabolite)

171-4(d)	Analytical Method (parent + metabolite)	44080354
171-4(e)	Storage Stability (soil)	44080355
171-4(k)	Crop trials: wheat, barley, and oats	44094904, 44080356, 44080357
171-4(l)	Processing Study: wheat	44080358
165-1	Confined Rotational Crops	44080350
N/A ·	Interpretive Summary of Residue Chemistry	y Data

All of the data packages listed above meet the basic acceptance criteria outlined in 40 CFR Part 158.340 and Part 158.240. The above studies can be assigned for review. Although the rotational crop study was conducted at 2.2X, the study passes the screen for review because of the low levels of residues detected in rotational crops. An FQPA Summary package was submitted. A previously submitted 28-day dog feeding study will be used to support the 90-day chronic feeding study (non-rodent) data requirement (82-1(b)).

Data have been submitted previously under an EUP for this chemical. All of the previously submitted toxicology data appear to have been reviewed under the EUP request as indicated on the data matrix sheet submitted with the new chemical screen package. However, it appears from the data matrix sheet that none of the residue chemistry studies previously submitted have been reviewed. HED recommends that RD confirm this, and if none of the residue chemistry data previously submitted have been reviewed, determine whether it should be screened prior to initiating a full review of this chemical.

cc: RCAB paper and electronic files

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## UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

# **MEMORANDUM**

EFED's New Chemical Screen for Fluroxypyr acid and Fluroxypyr, SUBJECT:

methylheptyl ester (Chemical #s 128959 and 128968; CAS #s 81406-37-3 and

69377-81-7; Case # 060640; DP Barcodes D230603 and D230920)

FROM:

Renee Costello, Biologist >

and

Stephanie K. Syslo, Environmental Scientist Environmental Risk Characterization Branch

Environmental Fate and Effects Division (7507C)

THRU:

Elizabeth M. Leovey, Chief

Environmental Risk Characterization Branch

Environmental Fate and Effects Division (75076)

TO:

Dan Kenny/Joanne Miller, PM 23

Registration Division (7505C)

ERCB/EFED has screened the environmental fate and ecotoxicology studies provided for the new Chemical Screen for the methylheptyl ester of Fluroxypyr (Chemical # 128968, Case # 060640) (see attached lists). The information provided to EFED passes the screen and can be put into full review. The studies provided for screening will be retained in ERCB pending initiation of the full review. A document that was included in the screen package (MRID 44080346) describing the analytical method used in the terrestrial field dissipation studies has been forwarded to BEAD as part of the environmental validation process (see attached memo).

#### **Summary of Data Reviews**

All of the basic ecological effects studies have been submitted, along with estuarine/marine, plants (both aquatic and terrestrial), and a chronic invertebrate study. Studies using both the ester and the acid forms as the test material were performed. A complete risk assessment could be performed with these data, provided the data are scientifically valid.

All the environmental fate studies required to support the proposed use (small grains = Terrestrial Food Crop) have been submitted. Studies were performed using only the ester as the test material; however, the fate of the fluroxypyr acid (the major metabolite) was well documented. A complete environmental fate assessment for the small grain use could be performed with these data, provided the data are scientifically valid.

# Background

Fluroxypyr, methylheptyl ester (1-methylheptyl(4-amino-3,5-dichloro-6-fluoro-2-pyridoxyl)acetate; Chemical # 128968) degrades rapidly to fluroxypyr acid (4-amino-3,5-dichloro-6-fluoro-2-pyridoxyl)acetic acid; Chemical # 128959); both forms are biologically active. In the documents provided for review, the registrant describes this herbicide as having a novel mode of action but does not describe it further.

The registrant DowElanco is proposing this chemical for use as a selective postemergence control of annual and perennial broadleaf weeds in wheat, barley, or oats (small grains not under-seeded with a legume), fallow cropland, and noncrop areas including industrial sites and rights-of-way such as electrical power lines, communication lines, pipelines, roadsides and railroads. It will be formulated as an EC with 26.2% fluroxypyr-MHE (1.5 lb fluroxypyr acid equivalent/gal) to be applied at a maximum rate of 0.25 lb ae/A applied by either aerial or ground equipment. There is also a registration request for the technical (98%).

The following data table summarizes the status of the ecotoxicology studies that were submitted specifically for this screen (all studies are reviewable):

Guideline number	MRID
72-3	. 44080309
72-3(a)	44080308
72-1(a)	44080307
72-3(c)	44080313
72-3	44080312
. 72-3(c)	44080311
72-3(b)	44080310
72-4	44080314
123-2	44080336
122-2 & 122-3	44080337
123-1	44080335
123-2	44080340
123-2	44080339
123-2	44080338

The following supplemental information was also submitted; these studies are not guideline requirements:

MRID	Title		
44080341	Evaluation of the phytotoxicity of 4-amino-3,5-dichloro-6-fluoro-2-methoxypyridine to the green algae Selenastrum capricornutum, Printz		
44080315	A review of the toxicity of fluroxypyr herbicide to fish and wildlife		
44094902	Phytotoxicity of fluroxypyr MHE and its metabolites fluroxypyr, methoxypyridine, and pyridinol to non-target terrestrial plants		

The following data table summarizes the status of the environmental fate documents that were evaluated specifically for this screen.

Guideline Number	MRID	Initiate review?	Comments
161-2	44080342	Reviewable	Photodegradation rates of ester and acid determined
161-3	44080343	Reviewable	Photodegradation rates of ester determined
162-3	44080344	Reviewable	Degradation rate not defined at 25°C but is defined at 5°C
162-4	44080345	Reviewable	Degradation rate not defined at 25°C but is defined at 5°C
163-1	44094903 ·	Reviewable	Involves degradates; unusual range of concentrations
164-1	44080347; 44080355	Reviewable	Storage stability data is crucial to determination of acceptability of data
165-4	44080348	Reviewable	Unusual approach to calculation of BCFs
Analytical method	· 44080346	-	Sent to Don Marlow for method validation

The following data table summarizes the status of additional environmental fate requirements based on documents that were previously reviewed by EFED.

Guideline · Number	MRID	Acceptability	Guideline Status
161-1	40244539	Acceptable	Satisfied
162-1	40244540 42137317, 42730001	Unacceptable Acceptable	Satisfied
163-1	40244541, 40244542, 40244543, 40244544 	Unacceptable  Partially acceptable	Data for degradates provided in MRID 44094903 (see above)



# UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT:

Fluroxypyr Analytical Method

FROM:

Elizabeth Leovey, Chief

Environmental Risk Characterization Branch

Environmental Fate and Effects Division (7507C)

TO:

Don Marlow, Chief

Analytical Chemistry Branch

Biological and Economic Analysis Division (7503W)

Attached please find an analytical method for the determination of fluroxypyr acid and its degradates in soil (GRM # 93.03). This document was part of the data package submitted by DowElanco as support for their application for registration of fluroxypyr, methylheptyl ester. Please evaluate this method as part of the environmental method validation process. In addition, could you please check your records for any evaluation work you may have done on another DowElanco method for determination of fluroxypyr, methylheptyl ester; the method number is ACR 91.10. Thank you.

#### Attachment:

Moore, M.G. 1996. Determination of residues of fluroxypyr ((4-amino-3,5-dichloro-6-fluoro-2-oxy acetic acid)pyridine), methoxypyridine ((4-amino-3,5-dichloro-6-fluoro-2-methoxy)pyridine), and 3,5-dichloro-6-fluoro-2-hydroxy)pyridine) in soil by capillary gas chromatography using mass selective detection. Method GRM # 93.03. Laboratory Study Identification GH-C 4170. Unpublished study performed and submitted by DowElanco, Indianapolis, IN. (MRID 44080346)

Reference:

VanDyke; M. 1991. Determination of residues of fluroxypyr methylheptyl ester in soil by gas chromatography/mass spectrometry. Method # ACR 91.10. Unpublished method of DowElanco.

757

DowElanco 9330 Zionsville Road Indianapolis, IN 46268-1054

308/2E October 25, 1996



Document Processing Desk Office of Pesticide Programs (7504C) U. S. Environmental Protection Agency Room 266A, Crystal Mall 2 1921 Jefferson Davis Highway Arlington, VA 22202

Attention: Mr. Daniel C. Kenny (7505C)

FLUROXYPYR MHE
PESTICIDE TOLERANCE PETITION; NOTICE OF FILING - FLUROXYPYR MHE
ON WHEAT, BARLEY AND OATS

Per our discussion, enclosed please find a hard copy and a disc containing the subject notice of filing to meet the requirements of the new FQPA.

#### Contents of Submission

- Transmittal document (this letter)
- Pesticide Tolerance Petition; Notice of Filing
   Fluroxypyr MHE on Wheat, Barley and Oats
   (1 3M HD/Formatted Disk)(WordPerfect 5.1/5.2 formatted)
- Pesticide Tolerance Petition; Notice of Filing Fluroxypyr MHE on Wheat, Barley and Oats dated October 25, 1996 (8 pages) (1 copy)

If you require further information, please contact me at the number listed below or Ms. Joyce Armstrong, Registration Assistant for this product, at (317) 337-4657.

Sincerely,

Robert F. Bischoff

Product Registration Manager

Robert P. Buchi

U.S. Regulatory, Toxicology and

**Environmental Chemistry** 

(317)-337-4686

(317) 337-4649 (FAX)

RFB/car

Enclosures

308/2E October 17, 1996



Document Processing Desk Office of Pesticide Programs (7504C) U. S. Environmental Protection Agency Room 266A, Crystal Mall 2 1921 Jefferson Davis Highway Arlington, VA 22202

Attention: Mr.Dan Kenny/Team 23 (7505C)

FLUROXYPYR METHYLHEPTYL ESTER (MHE)
PETITION FOR RESIDUE TOLERANCE ON WHEAT, BARLEY, AND OATS (PP 6F4772)
INFORMATIVE SUMMARY REQUIRED BY THE 1996 FOOD QUALITY PROTECTION ACT (FQPA)

Enclosed please find the subject fluroxypyr MHE informative summary. The format of this summary is based on the pyridaben time limited tolerance for an emergency exemption that appeared in the Federal Register on September 17, 1996. We trust that this summary meets the requirements of the new law.

#### Contents of Submission

- Transmittal document (this letter)
- Informative Summary required by the FQPA of 1996
   Petition for Use of Fluroxypyr Methylheptyl Ester (MHE) on Wheat.
   Barley, and Oats (PP 6F4772)
   dated October 7, 1996 (6 pages) (1 copy)

If you require further information, please contact me at the number listed below or Ms. Joyce Armstrong, Registration Assistant for this product. at (317) 337-4657.

Sincerely,

Robert F. Bischoff

Product Registration Manager U.S. Regulatory, Toxicology and

Environmental Chemistry

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RFB/car

Enclosures



# PETITION FOR USE OF FLUROXYPYR METHYLHEPTYL ESTER (MHE) ON WHEAT, BARLEY, AND OATS (PP 6F4772)

In compliance with Section 408 (d)(2)(A) of the new Food Quality Protection Act, the following informative summary is intended to support the pesticide petition (PP 6F4772) for use of fluroxypyr MHE on wheat, barley, and oats. Fluroxypyr MHE (the active ingredient) and fluroxypyr (the acid equivalent) are the common names for 1methylheptyl (4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyl)acetate and (4-amino-3,5dichloro-6-fluoro-2-pyridyloxy)acetic acid, respectively. Both the ester and acid forms of fluroxypyr have biological activity against various weed species. Fluroxypyr MHE is readily hydrolyzed to the acidic form; it undergoes a rapid hydrolysis to fluroxypyr in soil/water slurries with observed half-lives on the order of hours. Fluroxypyr is a nonphenoxy herbicide which induces auxin-type responses in susceptible broadleaf species. This new active ingredient is being proposed for registration as a postemergence broadleaf weed control product on wheat, barley, and oats. In addition, permanent tolerances for combined residues of fluroxypyr MHE and its only significant metabolite fluroxypyr, free and conjugated, all expressed as fluroxypyr, in or on wheat. barley, and oats are being proposed in support of this new registration as follows: 0.5 ppm (grain), 10 ppm (straw and forage), 20 ppm (hay), and 0.5 ppm (aspirated grain fractions, wheat). Because residues of fluroxypyr MHE or fluroxypyr, free and conjugated, may occur in animal feeds derived from wheat, barley, and oats, the following meat and milk tolerances are also being proposed: 0.1 ppm (meat, fat, milk, and meat byproducts except for kidney) and 0.5 ppm (kidney).

# Toxicological Profile

Acute Toxicity. Fluroxypyr MHE has low acute toxicity. The rat oral LD50 is >5000 mg/kg, the rabbit dermal LD50 is >2000 mg/kg, and the rat inhalation LC50 is >1.0 mg/l (1000 mg/cubic meter), the maximum attainable concentration. In addition, fluroxypyr MHE is not a skin sensitizer in guinea pigs, has no dermal irritation in rabbits, and shows mild ocular irritation in rabbits. The end use formulation of fluroxypyr MHE has a similar low acute toxicity profile.

Subchronic Toxicity. Fluroxypyr MHE showed a NOEL of 1000 mg/kg/day in a 90-day rat dietary study and a 21-day rabbit dermal study. Ninety day feeding studies with fluroxypyr showed NOELs of 80 mg/kg/day (Wistar rats), 700 mg/kg/day (Fischer 344 rats), 1342 mg/kg/day (male mice), and 1748 mg/kg/day (female mice). In a 4-week dietary, range finding study with fluroxypyr in dogs the NOEL was >50 mg/kg/day.

Teratology and Reproduction. Developmental studies in rats and rabbits were conducted with both fluroxypyr MHE and fluroxypyr. Studies with fluroxypyr MHE showed maternal and fetal NOELs of 300 mg/kg/day (rat) and 500 mg/kg/day (rabbit). Studies with fluroxypyr showed NOAELs in the rat of 250 mg/kg/day for maternal effects and 500 mg/kg/day for fetal effects and a NOEL in the rabbit of 250 mg/kg/day for both maternal and fetal effects. These studies show that fluroxypyr and fluroxypyr MHE are not teratogenic nor will they interfere with *in utero* development. Two multigeneration reproduction studies were conducted with fluroxypyr in rats. The first in Wistar rats showed no effect on fertility or reproductive performance and had a NOAEL of 500 mg/kg/day (highest dose tested). The second study in Sprague-Dawley rats showed a parental NOEL for systemic effects of 100 mg/kg/day in male rats and 500 mg/kg/day in female rats. The NOEL for reproductive effects was 750 mg/kg/day for males and 1000 mg/kg/day for females (highest dose tested). The NOEL for neonatal effects was 500 mg/kg/day.

Chronic Toxicity. Based on chronic testing with fluroxypyr in the mouse, dog, and rat (two studies), a reference dose (RfD) of 0.8 mg/kg/day is proposed for fluroxypyr and fluroxypyr MHE. The RfD has incorporated a 100-fold safety factor to the NOEL found in the rat chronic test. NOELs found in the chronic dietary studies are as follows: 150 mg/kg/day (dog). 300 mg/kg/day (mouse), 80 mg/kg/day (Wistar rats), 100 mg/kg/day (male Fischer 344 rats), and 500 mg/kg/day (female Fischer 344 rats).

Carcinogenicity. Using the Guidelines for Carcinogen Risk Assessment published September 24, 1986 (51 FR 33992), it is proposed that fluroxypyr and fluroxypyr MHE be classified as Group E for carcinogenicity (no evidence of carcinogenicity) based on the results of carcinogenicity studies in two species. There was no evidence of carcinogenicity in an 18-month mouse feeding study and a 24-month rat feeding study at all dosages tested. The NOELs shown in the mouse and rat oncogenicity studies were 1000 and 320 mg/kg/day. respectively. A maximum tolerated dose was achieved at the top dosage level tested in both of these studies based on excessive renal toxicity. Thus, the doses tested are adequate for identifying a cancer risk. Accordingly, a cancer risk assessment is not needed.

Mutagenicity. Short term assays for genotoxicity consisting of a bacterial reverse mutation assay (Ames test), an *in vitro* assay for cytogenetic damage using the Chinese hamster ovary cells, an *in vitro* chromosomal aberration assay using rat lymphocytes, and an *in vivo* cytogenetic assay in the mouse bone marrow (micronucleus test) have been conducted with fluroxypyr MHE. These studies show a lack of genotoxicity. In addition, short term assays for genotoxicity consisting of an Ames metabolic activation test, point mutations at the HGPRT-Locus of Chinese hamster ovary cells, *in vivo* and

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in vitro chromosomal aberrations in the Chinese hamster ovary cells, unscheduled DNA synthesis in human embryonic cells, and an assay in mouse lymphoma cells have been conducted with fluroxypyr. The weight of evidence also indicates a lack of genotoxicity.

Metabolism. Both fluroxypyr and fluroxypyr MHE have been evaluated in rat metabolism studies. In summary, these studies show that fluroxypyr MHE is rapidly hydrolyzed and the fate of the hydrolysis products, fluroxypyr and 1-methylheptanol, are independent of whether they were given as the ester or the acid. Fluroxypyr, per se, was extensively absorbed and rapidly excreted principally unchanged in the urine. 1-Methylheptanol also was rapidly absorbed and rapidly eliminated. Repeated administration of fluroxypyr MHE was not associated with accumulation in tissues. Also, the metabolism and pharmacokinetics of methylheptanol are comparable to that of the methylheptyl portion of fluroxypyr MHE.

Fluroxypyr MHE and Fluroxypyr Bioequivalency. Administration of fluroxypyr, as the acid or methylheptyl ester, in a variety of toxicological studies has produced similar effects. The principal response to sufficiently high dosages, whether administered over the short-term or, in some cases, over a lifetime, was nephrosis. Fluroxypyr is an organic acid that is actively excreted into the urine by the kidney. Thus, the target organ and dose response relationship for fluroxypyr toxicity are entirely consistent with the data on the toxicokinetics of fluroxypyr. Metabolism studies have shown that fluroxypyr MHE is rapidly and completely hydrolyzed to fluroxypyr acid and methylheptanol.

Endocrine Effects. There is no evidence to suggest that fluroxypyr and fluroxypyr HME have an effect on any endocrine system.

# Aggregate Exposure

Dietary. An over estimation of dietary exposure from use of fluroxypyr MHE on wheat, barley, oats is determined by basing the TMRC on the conservative assumptions that all cereal grain commodities will have tolerance level residues of fluroxypyr and that 100% of the wheat, barley, and oat crops grown in the U.S. are treated with fluroxypyr MHE. The TMRC is obtained by multiplying the tolerance residue levels by the consumption data which estimates the amount of crops and related feodstuffs consumed by various population subgroups. There are no other established U.S. tolerances or exemption from tolerances for fluroxypyr MHE and no other registered uses for fluroxypyr MHE on food or feed crops in the United States. The use of a tolerance level and 100% of crop treated clearly results in an overestimate of human

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exposure and a safety determination for the use of fluroxypyr MHE on wheat, barley, and oats that is based on a conservative exposure assessment.

Drinking Water and Non-Occupational. Other potential sources of exposure of the general population to residues of pesticides are residues in drinking water and exposure from non-occupational sources. Based on the available environmental studies conducted with fluroxypyr MHE and fluroxypyr wherein the properties of these materials show little persistence in the soil environment, there is no anticipated exposure to residues of fluroxypyr MHE and fluroxypyr in drinking water. In addition, there is no established Maximum Concentration Level for residues of fluroxypyr MHE and fluroxypyr in drinking water. There are no other uses currently registered for fluroxypyr MHE and fluroxypyr. The proposed use on wheat, barley and satisfivolves application of fluroxypyr MHE to crops grown in an agriculture drivironment. Thus, the potential for non-occupational exposure to the general population is not expected to be significant.

<u>Cumulative Effects.</u> The potential for cumulative effects of fluroxypyr MHE and fluroxypyr and other substances that have a common mechanism of toxicity is also considered. There is no reliable information to indicate that toxic effects produced by fluroxypyr MHE and fluroxypyr would be cumulative with those of any other pesticide chemical. Thus it is appropriate to consider only the potential risks of fluroxypyr MHE and fluroxypyr in an aggregate exposure assessment.

#### Safety Determinations

U.S. Population in General. Using the conservative exposure assumptions and the proposed RfD, the dietary exposure to fluroxypyr MHE use on wheat, bariey, and oats will utilize 0.2% of the RfD for the U.S. population. EPA generally has no concern for exposures below 100% of the RfD because the RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable ricks to human health. Since there are no anticipated residues in drinking water or from other non-occupational sources and no reliable information exists on cumulative effects due to common mechanism of toxicity, the aggregate exposure to fluroxypyr MHE is adequately represented by the dietary route. Thus, it is clear that there is reasonable certainty that no harm will result from aggregate exposure to fluroxypyr MHE residues on wheat, barley, and oats.

<u>Infants and Children.</u> In assessing the potential for additional sensitivity of infants and children to residues of fluroxypyr MHE, data from developmental toxicity studies in rats and rabbits and a 2-generation reproduction study in the rat are considered. The developmental toxicity studies are designed to evaluate adverse effects on the

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developing organism resulting from pesticide exposure during prenatal development. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability and potential systemic toxicity of mating animals and on various parameters associated with the well-being of pups.

FFDCA Section 408 provides that EPA may apply an additional safety factor for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database. Based on the current toxicological data requirements, the database for fluroxypyr MHE relative to pre- and post-natal effects for children is complete. Further, for fluroxypyr MHE, the NOEL in the chronic feeding studies which was used to calculate the RfD (0.8 mg/kg/day) is already lower than the NOELs from the developmental studies in rats and rabbits by a factor of more than 3.

Concerning the reproduction studies in rats, the pup effects shown at the highest dose tested (1000 mg/kg/day) were attributed to maternal toxicity. Therefore, it is concluded that an additional uncertainty factor is not needed and that the RfD at 0.8 mg/kg/day is appropriate for assessing risk to infants and children.

As noted above for the general U.S. population, aggregate exposure for infants and children will result from the dietary (i.e. not drinking water or non-occupational) route of exposure. In addition, there is no reliable information that shows cumulative effects based on a common mechanism of toxicity for infants and children. Using the conservative exposure assumptions previously described, the percent RfD utilized by the aggregate dietary exposure to residues of fluroxypyr MHE on wheat, barley, and oats is 0.6% for children 1 to 6 years old, the most sensitive population subgroup. Thus, based on the completeness and reliability of the toxicity data and the conservative exposure assessment, it is concluded that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to fluroxypyr MHE residues on wheat, barley, and oats.

#### Other Considerations

The metabolism of fluroxypyr MHE in plants (wheat) and animals (goats and poultry) is adequately understood for the purposes of this tolerance. A rotational crop study showed no carryover of significant fluroxypyr MHE related residues in representative test crops except for cereal grains for which tolerances are being proposed. Magnitude of residue studies were conducted for wheat, barley, and oats. Residues of fluroxypyr MHE did not concentrate in process fractions in samples treated at a 7.5X application. There is a practical method (GC with MS detection) for measuring levels of fluroxypyr MHE in or on food with a limit of detection that allows monitoring of food

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with residues at or above the levels set for the proposed tolerances. Fluroxypyr has been tested through the FDAs Multiresidue Methodology, Protocols C, D. and E. The results have been published in the FDA Pesticide Analytical Manual, Volume I. There are no Codex maximum residue levels established for residues of fluroxypyr MHE on any food or feed crop.

#### Conclusion

A permanent tolerance in connection with the FIFRA Section 3 registration for use of fluroxypyr MHE on wheat, barley, and oats meets the requirements of the new Food Quality Protection Act and thus should be established.

The undersigned, Robert F. Bischoff, Product Registration Manager, DowElanco, on behalf of DowElanco agrees that the above summary or any information it contains may be published as a part of the notice of filing of the petition to be published under FFDCA Section 408 and as part of a proposed or final regulation issued under the same Section.

Robert F. Bischoff

Product Registration Manager

DowElanco

October 16, 1996

Date

Created: RFB/10/7/96

Dow Plance 9330 Zionsviile Road Indianapolis, IN 46268-1054

308/2E October 16, 1996

Document Processing Desk Office of Pesticide Programs (7504C) U. S. Environmental Protection Agency Room 266A, Crystal Mall 2 1921 Jefferson Davis Highway Arlington, VA 22202



Attention: Mr. Adam Heyward/Team 13 (7505C) Team 23

FLUROXYPYR METHYLHEPTYL ESTER (MHE) PETITION FOR RESIDUE TOLERANCE ON WHEAT, BARLEY, AND OATS (PP 6F4772) INFORMATIVE SUMMARY REQUIRED BY THE 1996 FOOD QUALITY PROTECTION ACT (FQPA)

Enclosed please find the subject fluroxypyr MHE informative summary. The format of this summary is based on the pyridaben time limited tolerance for an emergency exemption that appeared in the Federal Register on September 17, 1996. We trust that this summary meets the requirements of the new law.

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If you require further information, please contact me at the number listed below or Ms. Joyce Armstrong, Registration Assistant for this product, at (317) 337-4657.

Sincerely,

Robert F. Bischoff

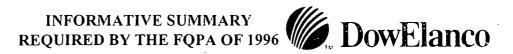
Product Registration Manager U.S. Regulatory, Toxicology and **Environmental Chemistry** (317) 337-4686

Robert F. Beschoff

(317) 337-4649 (FAX)

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Enclosures



## PETITION FOR USE OF FLUROXYPYR METHYLHEPTYL ESTER (MHE) ON WHEAT, BARLEY, AND OATS (PP 6F4772)

In compliance with Section 408 (d)(2)(A) of the new Food Quality Protection Act, the following informative summary is intended to support the pesticide petition (PP 6F4772) for use of fluroxypyr MHE on wheat, barley, and oats. Fluroxypyr MHE (the active ingredient) and fluroxypyr (the acid equivalent) are the common names for 1methylheptyl (4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyl)acetate and (4-amino-3,5dichloro-6-fluoro-2-pyridyloxy)acetic acid, respectively. Both the ester and acid forms of fluroxypyr have biological activity against various weed species. Fluroxypyr MHE is readily hydrolyzed to the acidic form; it undergoes a rapid hydrolysis to fluroxypyr in soil/water slurries with observed half-lives on the order of hours. Fluroxypyr is a nonphenoxy herbicide which induces auxin-type responses in susceptible broadleaf species. This new active ingredient is being proposed for registration as a postemergence broadleaf weed control product on wheat, barley, and oats. In addition, permanent tolerances for combined residues of fluroxypyr MHE and its only significant metabolite fluroxypyr, free and conjugated, all expressed as fluroxypyr, in or on wheat. barley, and oats are being proposed in support of this new registration as follows: 0.5 ppm (grain), 10 ppm (straw and forage), 20 ppm (hay), and 0.5 ppm (aspirated grain fractions, wheat). Because residues of fluroxypyr MHE or fluroxypyr, free and conjugated, may occur in animal feeds derived from wheat, barley, and oats, the following meat and milk tolerances are also being proposed: 0.1 ppm (meat, fat, milk, and meat byproducts except for kidney) and 0.5 ppm (kidney).

#### Toxicological Profile

Acute Toxicity. Fluroxypyr MHE has low acute toxicity. The rat oral LD50 is >5000 mg/kg, the rabbit dermal LD50 is >2000 mg/kg, and the rat inhalation LC50 is >1.0 mg/l (1000 mg/cubic meter), the maximum attainable concentration. In addition, fluroxypyr MHE is not a skin sensitizer in guinea pigs, has no dermal irritation in rabbits, and shows mild ocular irritation in rabbits. The end use formulation of fluroxypyr MHE has a similar low acute toxicity profile.

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(1) ...

Teratology and Reproduction. Developmental studies in rats and rabbits were conducted with both fluroxypyr MHE and fluroxypyr. Studies with fluroxypyr MHE showed maternal and fetal NOELs of 300 mg/kg/day (rat) and 500 mg/kg/day (rabbit). Studies with fluroxypyr showed NOAELs in the rat of 250 mg/kg/day for maternal effects and 500 mg/kg/day for fetal effects and a NOEL in the rabbit of 250 mg/kg/day for both maternal and fetal effects. These studies show that fluroxypyr and fluroxypyr MHE are not teratogenic nor will they interfere with *in utero* development. Two multigeneration reproduction studies were conducted with fluroxypyr in rats. The first in Wistar rats showed no effect on fertility or reproductive performance and had a NOAEL of 500 mg/kg/day (highest dose tested). The second study in Sprague-Dawley rats showed a parental NOEL for systemic effects of 100 mg/kg/day in male rats and 500 mg/kg/day in female rats. The NOEL for reproductive effects was 750 mg/kg/day for males and 1000 mg/kg/day for females (highest dose tested). The NOEL for neonatal effects was 500 mg/kg/day.

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Mutagenicity. Short term assays for genotoxicity consisting of a bacterial reverse mutation assay (Ames test), an *in vitro* assay for cytogenetic damage using the Chinese hamster ovary cells, an *in vitro* chromosomal aberration assay using rat lymphocytes, and an *in vivo* cytogenetic assay in the mouse bone marrow (micronucleus test) have been conducted with fluroxypyr MHE. These studies show a lack of genotoxicity. In addition, short term assays for genotoxicity consisting of an Ames metabolic activation test, point mutations at the HGPRT-Locus of Chinese hamster ovary cells, *in vivo* and

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in vitro chromosomal aberrations in the Chinese hamster ovary cells, unscheduled DNA synthesis in human embryonic cells, and an assay in mouse lymphoma cells have been conducted with fluroxypyr. The weight of evidence also indicates a lack of genotoxicity.

Metabolism. Both fluroxypyr and fluroxypyr MHE have been evaluated in rat metabolism studies. In summary, these studies show that fluroxypyr MHE is rapidly hydrolyzed and the fate of the hydrolysis products, fluroxypyr and 1-methylheptanol, are independent of whether they were given as the ester or the acid. Fluroxypyr, per se, was extensively absorbed and rapidly excreted principally unchanged in the urine. 1-Methylheptanol also was rapidly absorbed and rapidly eliminated. Repeated administration of fluroxypyr MHE was not associated with accumulation in tissues. Also, the metabolism and pharmacokinetics of methylheptanol are comparable to that of the methylheptyl portion of fluroxypyr MHE.

Fluroxypyr MHE and Fluroxypyr Bioequivalency. Administration of fluroxypyr, as the acid or methylheptyl ester, in a variety of toxicological studies has produced similar effects. The principal response to sufficiently high dosages, whether administered over the short-term or, in some cases, over a lifetime, was nephrosis. Fluroxypyr is an organic acid that is actively excreted into the urine by the kidney. Thus, the target organ and dose response relationship for fluroxypyr toxicity are entirely consistent with the data on the toxicokinetics of fluroxypyr. Metabolism studies have shown that fluroxypyr MHE is rapidly and completely hydrolyzed to fluroxypyr acid and methylheptanol.

Endocrine Effects. There is no evidence to suggest that fluroxypyr and fluroxypyr HME have an effect on any endocrine system.

#### Aggregate Exposure

<u>Dietary.</u> An over estimation of dietary exposure from use of fluroxypyr MHE on wheat, barley, oats is determined by basing the TMRC on the conservative assumptions that all cereal grain commodities will have tolerance level residues of fluroxypyr and that 100% of the wheat, barley, and oat crops grown in the U.S. are treated with fluroxypyr MHE. The TMRC is obtained by multiplying the tolerance residue levels by the consumption data which estimates the amount of crops and related foodstuffs consumed by various population subgroups. There are no other established U.S. tolerances or exemption from tolerances for fluroxypyr MHE and no other registered uses for fluroxypyr MHE on food or feed crops in the United States. The use of a tolerance level and 100% of crop treated clearly results in an overestimate of human

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exposure and a safety determination for the use of fluroxypyr MHE on wheat, barley, and oats that is based on a conservative exposure assessment.

Drinking Water and Non-Occupational. Other potential sources of exposure of the general population to residues of pesticides are residues in drinking water and exposure from non-occupational sources. Based on the available environmental studies conducted with fluroxypyr MHE and fluroxypyr wherein the properties of these materials show little persistence in the soil environment, there is no anticipated exposure to residues of fluroxypyr MHE and fluroxypyr in drinking water. In addition, there is no established Maximum Concentration Level for residues of fluroxypyr MHE and fluroxypyr in drinking water. There are no other uses currently registered for fluroxypyr MHE and fluroxypyr. The proposed use on wheat, barley, and oats involves application of fluroxypyr MHE to crops grown in an agriculture environment. Thus, the potential for non-occupational exposure to the general population is not expected to be significant.

<u>Cumulative Effects.</u> The potential for cumulative effects of fluroxypyr MHE and fluroxypyr and other substances that have a common mechanism of toxicity is also considered. There is no reliable information to indicate that toxic effects produced by fluroxypyr MHE and fluroxypyr would be cumulative with those of any other pesticide chemical. Thus it is appropriate to consider only the potential risks of fluroxypyr MHE and fluroxypyr in an aggregate exposure assessment.

#### Safety Determinations

O.S. Population in General. Using the conservative exposure assumptions and the proposed RfD, the dietary exposure to fluroxypyr MHE use on wheat, barley, and oats will utilize 0.2% of the RfD for the U.S. population. EPA generally has no concern for exposures below 100% of the RfD because the RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Since there are no anticipated residues in drinking water or from other non-occupational sources and no reliable information exists on cumulative effects due to common mechanism of toxicity, the aggregate exposure to fluroxypyr MHE is adequately represented by the dietary route. Thus, it is clear that there is reasonable certainty that no harm will result from aggregate exposure to fluroxypyr MHE residues on wheat, barley, and oats.

Infants-and Children. In assessing the potential for additional sensitivity of infants and children to residues of fluroxypyr MHE, data from developmental toxicity studies in rats and rabbits and a 2-generation reproduction study in the rat are considered. The developmental toxicity studies are designed to evaluate adverse effects on the

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developing organism resulting from pesticide exposure during prenatal development. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability and potential systemic toxicity of mating animals and on various parameters associated with the well-being of pups.

FFDCA Section 408 provides that EPA may apply an additional safety factor for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database. Based on the current toxicological data requirements, the database for fluroxypyr MHE relative to pre- and post-natal effects for children is complete. Further, for fluroxypyr MHE, the NOEL in the chronic feeding studies which was used to calculate the RfD (0.8 mg/kg/day) is already lower than the NOELs from the developmental studies in rats and rabbits by a factor of more than 3.

Concerning the reproduction studies in rats, the pup effects shown at the highest dose tested (1000 mg/kg/day) were attributed to maternal toxicity. Therefore, it is concluded that an additional uncertainty factor is not needed and that the RfD at 0.8 mg/kg/day is appropriate for assessing risk to infants and children.

As noted above for the general I.S. population, aggregate exposure for infants and children will result from the dietary (i.e. not drinking water or non-occupational) route of exposure. In addition, there is no reliable information that shows cumulative effects based on a common mechanism of toxicity for infants and children I lising the conservative exposure assumptions previously described, the percent Republic why the aggregate dietary exposure to residues of fluroxypyr MHE on wheat, bariey, and oats is 0.6% for children 1 to 6 years old, the most sensitive population subgroup. Thus, based on the completeness and reliability of the toxicity data and the conservative exposure assessment, it is concluded that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to fluroxypyr MHE residues on wheat, barley, and oats.

#### Other Considerations

The metabolism of fluroxypyr MHE in plants (wheat) and animals (goats and poultry) is adequately understood for the purposes of this tolerance. A rotationa: crop study showed no carryover of significant fluroxypyr MHE related residues in representative test crops except for cereal grains for which tolerances are being proposed. Magnitude of residue studies were conducted for wheat, barley, and oats. Residues of fluroxypyr MHE did not concentrate in process fractions in samples treated at a 7.5X application rate. There is a practical method (GC with MS detection) for measuring levels of fluroxypyr MHE in or on food with a limit of detection that allows monitoring of fcod

Created: RFB/10/7/96 FN: Fluroxypyr Info Sum 10-16.doc with residues at or above the levels set for the proposed tolerances. Fluroxypyr has been tested through the FDAs Multiresidue Methodology, Protocols C, D. and E. The results have been published in the FDA Pesticide Analytical Manual, Volume I. There are no Codex maximum residue levels established for residues of fluroxypyr MHE on any food or feed crop.

#### Conclusion

A permanent tolerance in connection with the FIFRA Section 3 registration for use of fluroxypyr MHE on wheat, barley, and oats meets the requirements of the new Food Quality Protection Act and thus should be established.

The undersigned, Robert F. Bischoff, Product Registration Manager, DowElanco, on behalf of DowElanco agrees that the above summary or any information it contains may be published as a part of the notice of filing of the petition to be published under FFDCA Section 408 and as part of a proposed or final regulation issued under the same Section.

Robert F. Bischoff

Product Registration Manager

DowElanco ·

October 16, 1996

Date

Created: RFB/10/7/96

308/2E August 23, 1996



Document Processing Desk
Office of Pesticide Programs (7504C)
U. S. Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Attention: Ms. Joanne I. Miller/PM-23 (7505C)

FLUROXYPYR: PP#6F4772

EPA FILE SYMBOL NUMBER: STARANE\* F (62719-EIL) EPA FILE SYMBOL NUMBER: STARANE\* EC (62719-EIA)

RESPONSE TO DATA FORMAT DEFICIENCIES ON SUBMISSION DATED AUGUST 6, 1996

Attached please find three copies of all corrections to the data format deficiencies noted on your fax dated August 21, 1996. These corrections are listed below.

Correction	Volume No.	Study		
MISSING Pages 111-156	Volume 19 83-3	A Developmental Toxicity Stu Methylheptyl Ester	udy in Rats w/Fluroxypyr	
	2	Schroeder, R.E.	May 3, 1994	
		Study ID: 93-4052	(K-137992-007)	
STATEMENT CORRECTED on GLP Page 3 (Includes Revised Summary Page (1R of 2). Study Title Page (1R of 200), GLP Page (3R), QA Page (4R), and addition of Page 4.1)	Volume 44 N/A		MHE and its Metabolites Fluroxypyr, nol to Non-Target Terrestrial Plants  Nov. 20, 1995 (Aug. 23, 1996)	
MISSING Page 86	Volume 49 163-1	Adsorption/Desorption Batch Methoxypyridine and Dichlord Cleveland, C.B. Study ID: ENV95072	Equilibrium Partitioning of opyridinol Metabolites of Fluroxypyr February 29, 1996 GH-C 3854	

<sup>\*</sup>Trademark of DowElanco

Ms. Joanne I. Miller/PM-23 (7505C) RESPONSE TO DATA FORMAT DEFICIENCIES ON SUBMISSION DATED AUGUST 6, 1996 August 23, 1996 Page 2

Correction	Volume No.	Study	
MISSING Page 83	Volume 60 171-4(k)	The Magnitude of Residue of Postemergence Application o	Fluroxypyr in Wheat Following f XRM-5316
		Roberts, D.W. Study ID: RES95051	July 10, 1996 (July 24, 1996) GH-C 4063

If you require further information, please contact me at the number listed below or Joyce Armstrong, Registration Assistant for this product, at (317) 337-4657.

Sincerely,

Robert F. Bischoff

Product Registration Manager U.S. Regulatory, Toxicology and Environmental Chemistry

Robert F. Beschoff 2

(317) 337-4686

(317) 337-4649 (FAX)

RFB/jla

Enclosures

308/2E August 6, 1996

Document Processing Desk (APPL/PETN)/6(a)(2)
Office of Pesticide Programs (7504C)
U. S. Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Attention: Ms. Joanne I. Miller/PM-23 (7505C)

STARANE\* F (TECHNICAL) AND STARANE EC (END-USE)
(A.I. FLURONYPYR METHYLHEPTYL ESTER (MHE))
EPA FILE SYMBOL NUMBERS: 62719-XXX
ÁFPLICATIONS FOR NEW REGISTRATION - SECTION 3

PETITION FOR PERMANENT TOLERANCE- FOR FLUROXYPYR METHYLHEPTYL ESTER (MHE) RESIDUES ON WHEAT, BARLEY AND OATS

DowElanco is respectfully submitting an application for new registration for Starane F heroicide (a technical product) and Starane EC heroicide (an end use product for use on wheat, barley, oats, fallow cropland and non-cropland), which contains fluroxypyr MHE. A petition for permanent tolerance for residues of fluroxypyr MHE and fluroxypyr on wheat, barley and oats accompanies this application.

A check to cover petition fees in the amount of \$61,950.00 (check # 53064046) has been mailed under separate cover letter dated August 6, 1996. A complimentary copy is enclosed in the transmittal document.

DowElanco desires approval of the enclosed permanent tolerance petition and acceptance of the proposed Section 3 registration's for Staranc Fland Starance EC on or before January 31, 1998.

Contents of Subspission

Volume 1 (Administrative) Transmittal document (this letter)
General Summaries for Public Release (63)

Application for Pesticide, EPA Form 8570-1 for Starane F (OPP No. 243062)

Application for Pesticide, EPA Form 8570-1 for Starane EC (OPP No. 249024)

Certification with Respect to Citation of Data for Starane F

Certification with Respect to Citation of Data for Starane EC

Confidential Statement of Formula entitled Starane F (Basic/62719-XXX/06-24-96) (Pages 1 - 2) (2 originals)

Confidential Statement of Formula entitled Starane EC (Basic/62719-XXX/06-10-96) (Pages 1 - 2) (2 originals)

Ma DowElanco

RECO ENVIOREMENTOR

Four studies will be flagged to be submitted for 6(a)(2) consideration.

<sup>\*</sup> Trademark of DowElanco

Volume 1 (cont'd)

Complimentary Copy: DowElanco letter to EPA dated
August 6, 1996, with check # 53064046 to cover Tolerance Fees.

Proposed label entitled Starane F (Technical)
(B2A/Starane F/PropSec3/07-11-96) (Pages 1 - 2) (5 cepies)

Proposed label entitled Starane EC (End Use)
(B2A/Starane EC/PropSec3/97-29-96) (Pages 1 - 10) (5 copies)

Data Matrix emitted Fluroxypy r MHE & 222 August 6, 1996 (Pages 1 - 18)(1 copy)

Petition for Permanent Tolerance for Residue of Fluroxypyr MHE and Fluroxypyr on Wheat, Barley and Oats

Includes Complimentary Copies of:

Proposed labeling entitled Starane F (2 copies) (B2A/Starane F/PropSec3/07-11-96) (Pages 1 - 2)

Proposed labeling entitled Starane EC (2 copies)
(B2A/Starane EC/PropSec3/07-29-96) (Pages 1 - 10)

Data Matrix for Fluroxypyr MilE (includes studies previously submitted as well as studies included with this submission dated August 6, 1996) (Pages 1 - 18) (2 copies)

Complimentary Copy (adds supplemental information to the fluroxypyr MHE environmental fate profile):

Aerobic Soil Metabolism of 12C-Fluroxypyr-MHE

Ballatine, Larry G. Ph.D.

January 5, 1993

Study ID: ENV92015

GH-C # 3033

Pages: 1-115

(1 copy) (Guideline No. 162-3)

#### Product Chemistry (Technical/Starane F)

Volume Guidelin		MRID No.	Contents	· :			
Volume 2 Series 61	UYO	8030/	. Series 61: Produ	Series 61: Product Identity and Composition of STARANE* Herbicide			
	110	•	Paterson, E.S.		July 15, 1996		
•			Stedy ID: GH-	C # 4145	(Confidential Attachment pgs 1-38)		
			Pages: 1-3		(3 copies)		
Volume 3 Series 62	440	90302	•		on of Product ingredients of echnical Grade of Active Ingredient		
			Ghaoui, L.H.		July 22, 1996		
			Study ID: GH-	C # 4141	(Confidential Attachment pgs 1-316)		
			Pages: 1-77		(3 copies)		
Volume 4 Series 63	440	780303			Characteristics of the Technical approximation of the Technica		
			Gi:aoui, L.H. Study ID: GH-		June 25, 1906		
			Pages: 1- 150		(3 copies)		

#### Product Ches Istry (End-Use/Stars in EC)

Volume 5 Series 61	44080304	Series 61: Product Identity and Composition of STARANE Herbicide, An Emulisifiable Concentrate Formulation of Fluroxypyr-1-Methylheptyl Ester			
		Paterson, E.S.	July 8, 1996		
	•	Study ID: GH-C # 4061	(Confidential Attachment pgs 1-47)		
		Pages: 1- 8	(3 copies)		
Volume 6 Series 62	44080305	Series 62: Analysis and Certification Use Product XRM-5316, and Emulsi Fluroxypyr-1-methylheptyl Ester (1-)	flable Concentrate Containing		
	•	Ghaoui, L.	July 17, 1996		
		Study ID: GH-C # 4033	(Confidential Attachment pgs 1-4)		
	•	Pages: 1- 27	(3 copiපා)		
Volume 7 Series 63	44080306	Series 63: Determination of Physical XRM-5316, and Emulsifiable Conce Methylheptyl Ester (1-MHE)	·		
		Kinnunen, C.A.	August 16, 1993		
		Study ID: FOR93081			
		Pages: 1- 15	(3 copies)		

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#### Wildlife and Aquatic Organisms

Volume i Guideline		Contents	
Volume 8 72-1(a)	44080307	Evaluation of the Acute Toxicity of F the Bluegill, Lepomis macrochirus R Rick, D.L. et. al * Study ID: DECO-ES-3020 Pages: 1-33	
Volume 9 72-3(a)	44080308	Fluroxypyr 1-Methylheptyl Ester: A Minnow, Cyprinodon variegatus Beeri, R.L. et.al Study ID: 707-DO Pages: 1-24	January 15, 1996 DECO-ES-2961 (3 copies)
Volume 10 72-3 (a)	44080309	Fluronypyr: Acute Toxicity to the Si Boeri, R.L. et. al Study ID: 199-DO (ES-2644) Pages: 1- 26 (3 copies)	February 4, 1994 DECO-ES-2644 (Amendad date June 8, 1994)
Voieme 11 72-3 (b)	44080310	Finite sypty: 1-Mathythoptyi Esteri: A Deposition Test Boeri, R.L. et. al Study ID: 646-DO Pages: 1-28	cute Flew-Through Melfase Shell January 12, 1996 DECO-ES-2925 (3 copies)
Volume 12 72-3(b)	44080311	Fluroxypyr: Acute Flow-through M Boeri, R.L. et.al Study ID: 198-DO (ES-2645) Pages: 1-25	February 3, 1994 DECO-ES-2645 (3 copies)
Volume 13 72-3(c)	44080312	Fluroxypyr: Acute Toxicity to the C Bocri, R.L. et. al Study ID: 197-DO (ES-2643) Pages: 1-24	February 14, 1994 DECO-ES-2643 (3 copies)
Volume 14 72-3(c)	44080313	Fluroxypyr 1-Methylheptyl Ester: A Palaemonetes pugio Boeri, R.L. et. al Study ID: 706-DO Pages: 1-24 (3 copies)	·.

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Evaluation of the Chronic Toxicity of Fluroxypyr 1-Methylheptyl Ester to the Daphnid, Daphnia megna STRAUS

Kirk, H.D. et.al

July 15, 1996

Study ID: DECO-ES-3079

Pages: 1-78

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Votume 16 44080315

A Review of the Toxicity of Fluroxypyr Herbicide to Fish and Wildlife

Maves, M. A.

Study ID: DECO-ES-3150

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July 31, 1996

Pages: 1-50

(3 copies)

#### Mammalian Toxicology

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Fluroxypyr: 13-Week Dietary Toxicity Study and 4-Week Recovery

Fluroxypyr: 18-Month Dietary and Oncogenicity Study in CD-1 Mice

Study in Fischer 344 Rats

Grundjean, M. chal

June 24, 1 92

Study ID: K-129976-667

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44080317 --- Volume 18 83-2

Cosse, P.F. et.al

July 20, 1993

Study ID: K-129976-004

Pages: 1-994

(3 copies)

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44094901

A Developmental Toxicity Study in Rats w/Fluroxypyr Methylheptyl

Ester

Schroeder, R.E.

May 3, 1094

Study ID: 93-4052

(K-137992-007)

Pages: 1-461

(3 copies) (No FOI pages)

44080318 Volume 20 N/A

A Range-Finding Study to Evaluate the Developmental Toxicity Study of Fluroxypyr Methylheptyl Ester in the Rat

Schroeder, R. E.

May 3, 1994

Study ID: 93-4051

(K-137992-006)

Pages: 1- 212

(3 copies)(No FOI pages)

#### Mammalian Toxicology (continued)

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44080319

Fluroxypyr Methylneptyl Ester: Oral Gavage Teratology Study in New

Zealand White Rabbits Liberacki, A. B. et. al

May 2, 1996

Study ID: K-137992-013

Pages: 1- 239

(3 copies)

44030320

- N/A

Flurexvovr Methylhoptyl Ester: Oral Gayage Teratology Probe Study in

New Zealand White Rubbits

Liberacki, A.B. et. al

May 2, 1996

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Fluroxypyr: Two Generation Dietary Reproductive Toxicity Study in

Sprague-Dawley Rats

Vedula, U. et.al.

June 19, 1996

Study ID: K-129976-012

Pages: 1-996

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Fischer 344 Rats - Final Report

Quast, J.F. et.al

June 15, 1995

Study ID: K-129976-008(1)

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44080323

Mutagenicity Test with Fluroxypyr Methylbeptyl Ester in the Salmonella -Escherichia Coli/Mammalian-Microsome Reverse Mutation

Assay Preincubation Method with a Confirmatory Assay

Lawlor, T. E.

December 28, 1995 (K-129976-008)

Study ID: 16848-0-422R Pages: 1-38

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Evaluation of Flurexypyr Methylheptyl Ester in the Chinese Hamster

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(CHO/HGPRT) Forward Mutation Assay

Linscombe, V.A. et.al

January 25, 1996

Study ID: K-137992-009

Pages: 1-39

(3 copies)

4408032 Volume 27 54-2

Evaluation of Floroxypyr Methylheptyl Ester in an In Viras Chromosomal Aberration Assay Utilizing Rat Evalphocytes Linscombe, A.V. et. al. January 16, 1996

Study ID: K-137992-010

Pages: 1-42

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44080326 Volume 28 84-2

Evaluation of Fluroxypyr Methylheptyl Ester in the Mouse Bone

Marrow Micronucleus Test

Lick, S.J. et.al

January 15, 1996

-Study ID: K-137992-011

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Fluroxypyr Methylheptyl Ester (Fluroxypyr MHE) and Methylheptanol:

Mount plism in Male Fischer 344 Rats District Programme 1

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rana R. i. iti

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A Review of the Mammalian Toxicity of Fluroxypyr and Fluroxypyr 1-Methylheptyl Ester

Eisenbrandt, D. L.

July 31, 1996

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November 20, 1992

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•		Cosse, P.F. <i>et.al</i> Study ID: M-005316-001D	November 20, 1992
		Pages: 1- 29	(3 copics)
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		Beckman, M.J. et.al Study ID: M-005316-002	February 18, 1993
		Pages: 1-35	(3 copies <sub>i</sub>
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		Cosse, P.F. et.al Study ID: NI-005316-001C	November 20, 1992
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		Pages: 1- 15	(3 copies)
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	r	Cossc, P.F. <i>et.al</i> Study ID: M-005316-001E	November 20, 1992
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#### Plant Protection

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Schwab, D. Study ID: RES95175 May 7, 1996 CH-C = 4033

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Fluroxypyr 1-Methylheptyl Ester: The Toxicity to the Blue-Green Alga. Anabaena flos-aquae

Milazzo, D.P. et.al

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Alexander, M.M.

May 31, 1996

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Duckweed Lemma Gibba L.G-3

Kirk, H.D. et.al

June 4, 1996

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Fluroxypyr I-Methylheptyl Ester: The Toxicity to the Freshwater Diatom, Navicula pelliculosa

Milazzo, D.P. et.al

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Kirk, H.D. et.al

October 6, 1995

Study ID: DECO-ES-3029

Pages: 1-15

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N/A

Phytotoxicity of Fluroxypyr MHE and its Metabolites Fluroxypyr. Methoxypyridine, and Pyridinol to Non-Target Terrestrial Plants

Wright, J. P. et. al

November 20, 1995

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#### Environmental Fate

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Cleveland, C.B. et al.

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44080343 Volume 46 161-3

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Batzer, F. R. et. al

March 3, 1992 (July 31, 1996)

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Anaerobic Aquatic Metabolism of Fluroxypyr Methylheptyl Ester

Cleveland, C.B. et.al

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Aerobic Aquatic Metabolism of Fluroxypyr Methylheptyl Ester

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June 24, 1993 GH-C # 3008

Study ID: ENV91075 Pages: 1- 125

(3 copies)

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Adsorption/Desorption Batch Equilibrium Partitioning of

Methoxypyridine and Chichlorepyridinol Metabolites of Fluroxypyr

Cleveland, C.B. et. al Stody ID: ENV95072

Pages: 1- 150

February 29, 1996 GH-C # 3854

(3 copies)

Volume 50 44080346

Determination of Residues of Fluroxypyr ((4-Amino-3.5-dichloro-6fluoro-2-oxy Acetic Acid)Pyridine), Methoxypyridine ((4-Amino-3.5dichlore-6-fluore-2-methoxy) Pyridine) and 2.5-Dichloropyridinol ((4-Amino3,5-dichloro-6-fluoro-2-hydroxy) Pyridine) in Soil by Capillary Gas Chromatography Using Mass Selective Detection

Moore, M.G.

Study ID: GH-C # 4170

Parris, 1-63

August 2, 1996

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Poletika, N.N. et.al

March 21, 1996

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GH-C # 3950

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The Bioconcentration and Metabolism of Fluroxypyr 1-Methylheptyl

Ester by the Rainbow Trout, Oncorhynchus mykiss Walbaum Rick, D.L. et.al

Study ID: DECO-ES-2679

June 13, 1996

Pages: 1-90

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Environmental Assessment/Summary of Fluroxypyr

Cleveland, C.B. et. al.

July 2, 1996

Study ID: GH-C 4034

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#### Residue Chemistry

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MRID No.

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A Confined Rotational Crop Study with <sup>14</sup>C-Fluroxypyr Methylheptyl

Yackovich, P.R. et.al Study ID: MET92057

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May 8, 1996 GH-C # 3988 (3 copies)

Volume 35 44980357

Nature of Residue of [15C] fluroxypyr in Luctating Gents

Huskin, M.A. Study ID: RES95025 May 29, 1996 GH-C # 3954

Pages: 1- 142

Pages: 1-231

(3 copies)

Volume 56 440 \$03 52 17!-4(c)

Validation Report for the Determination of Residues of Fluroxypyr and Fluroxypyr 1-Methylheptyl Ester as the Acid Equivalent in the Grain, Forage, Straw, and Hay of Wheat, Barley, and Oats by Capillary Gas Chromatography with Mass Selective Detection

Oldberding, E.L. et.al Study ID: RES95118 June 4, 1996 GH-C # 4049

Pagast I- Ch

(3 copies)

Volume 57 44080353

Independent Laboratory Validation of Method GRM 96.02 - Determination of Residues of Flurosypyr and Flurosypyr 1-Methylheptyl Ester as the Acid Equivalent in the Grain, Forage, Straw, and Hay of Wheat, and Oats by Capillary Gas Chromatography with Mass Selective Detection

McKellar, R.L. et. al Study ID: RES96044 August 2, 1996 GH-C # 4166

Pages: 1 - 85

(3 copies)

Volume 58 440 80354

Validation Report for the Determination of Residues of Fluroxypyr in Ruminant Tissues and Milk by Capillary Gas Chromatography with

Mass Selective Detection Olberding, E.L. *et.al* 

June 10, 1996

Study ID: RES95164

GH-C # 4048

Pages: 1- 59

(3 copies)

Volume 59 44080355

Frozen Storage Stability Study of Fluroxypyr 1-Methylheptyl Ester, Fluroxypyr, 4-amino-3,5-dichloro-6-fluoro-Pyridinol and 4-amino-3,5-dichloro-6-fluoro-Methoxypyridine in Soil

Phillips, A.M. et.al

May 29, 1996 GH-C # 4032

Sindy ID: RES93010/ RES93051

Pages: 1-112 -

(3 copies)

Section 3 for Fluroxypyt 8-6,doc

#### Residue Chemistry (continued)

Volume Guidelin		MRID No.	Contents	-	
Volume 60 171-4(k)	444	94904	The Magnitude of Residue of Fluro Postemergence Application of XRA		
-			Roberts, D. W. et.al	July 10, 1996 (July 24, 1996)	
			Study ID: RES95051	GH-C # 4063	
			Pages: 1- 212	(3 copies)	
Volume 61 171-4(k)	44.	580356	The Magnitude of Residue of Fluroxypyr in Barley Following Postemergence Application of XRM-5316		
			Robert, D. W. et. al	July 12, 1996 (July 24, 1996)	
			Study ID: RES95051.1	•	
			Pages: 1- 171	(3 copies)	
Volume 62 171-4(k)	44	080357	The Magnitude of Residue of Fluro Postemergence Application of XRN		
			Roberts, D. W., et. al	July 10, 1996 (July 24, 1996)	
		•	Study ID: RES95051.2	GH-C # 4065	
			Pages: 1- 189	(3 copies)	
Volume 63 171-4(1)	44	080356	Determination of Residues of Flure	xypyr in Wheat Processed Fractions	
• •			Phillips, A.M. et.al	January 27, 1995 (May 23, 1996)	
•			Study ID: RES93032	GH-C # 3477	
			Pages: 1- 87	(3 copies)	
			<u>-</u>		

ા છે. તેમાં કરાયું સુધારોને ઉપયોગ્નિક કેવાની હોય છે. જે જે જે માટે જે જે જે કોઈ કે જે જે જે જે જોઈ છે. જે જે જ

#### Tolerance Petition (Sections E. F & G)

Volume 64 171-5, 6, 7

ADMIN

Fluroxypyr in or on Barley, Oats and Wheat: Sections E, F and G of the

Petition for Permanent Tolerances.

July 30, 1996

Hamburg, A. W Study ID: GH-C 4159

Pages: 1- 29

(3 copies)

Volume 65 N/A 44080359

Interpretive Summary of Fluroxypyr and Fluroxypyr 1-Methylheptyl

Ester Residue Chemistry

Olberding, E. L.

August 2, 1996.

Study ID: GH-C 4158

Pages: 1- 32

(3 copies)

If you require further information, please contact me at the number listed below or Ms. Joyce Armstrong, Registration Assistant for this product, at (317) 337-4657.

Sincerely,

Robert F. Bischoff

Product Registration Manager

U.S. Regulatory, Toxicology and

**Environmental Chemistry** 

(317) 337-4686

(317) 337-4649 (FAX)

RFB/car

Enclosures

## U.S. ENVIRONMENTAL PROTECTION AGENCY Office of Pesticide Programs

DOWELANCO 9330 ZIONSVILLE ROAD INDIANAPOLIS, IN 462681054

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 08/26/96. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

NIFT Please lead instructions	on reverse before completin	g form.	F	orm Approv	∕ed. O	MB No. 20	<u>70-006</u> 0.	Approval e	xpires 05-31-
<b>≎EPA</b>	Environmental I	Protection A			X P	legistra Imendn Other	tion	OPP Identi	fier Number
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4. Company/Product (No. DowElanco,	ame)		PM#	23			X	None	Restricted
D <u>o</u> wElanco 9330 Zione Indianapo	Applicant (Include ZIP Code sville Road Lis, IN 46268 This is a new address		(b)(i), my to: EPA Reg Product	product is				FIFRA Section a	tion 3(c)(3) and labeling
	<u>.</u>	S	ection - II						
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		Se	ction - IV						
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Name Robert	F. Bischoff	Title Pro	duct Regis	stration	n Man	ager	•	• No. (Includ 337-468)	le Area Code) 6
	statements I have made on that any knowingly false or mis able law.							8. Date Ap Received (Sta	
2. Signature	,	3. Titl	•						
Robert (	F. Buch M	Pro	duct Regis	stration	Man	ager			

5. Date

Robert F. Bischoff

August 6, 1996

## EPA

#### United States

# Environmental Protection Agency RECD, SPA (SPE) Washington, DC 20460

Certification with Respect to Citation of Data

Form Approved OMB No. 2070-0060

Applicants Name and Address	<b>'</b> 96	AUG -8	P12:54	EPA File Symbol/Registration Nur	nber 62719-モエレ
DowElanco				Product Name	
9330 Zionsville Road					Starane F
Indianapolis, IN 46268				Date of Application	_
				1	August 6, 1996
				ered product that you purcha exemption Statement (EPA F	ise, and is labeled for the same uses, you form 8570-27)
				•	e-all options are indicated, this application
is supported by all and that is one of t identical or similar	data in the Agency's ne types of data tha composition and into	s files that c t would be r ended uses	oncem the proper required to be s under the data	perties of effects of this production submitted if this application se	uct that is identical or substantially similar ought the initial registration of a product of e date of approval of this application.
	h study cited in sup original submitter*; (	-	application for	registration that is an exclusi	ve use study.
I have ob	tained the written pe	ermission o	f the original su	bmitter for	, which is
		(1	for multiple che	micals link the companies w	ho are original data submitters
with the a	(insert names of companies) appropriate chemica	I name) to d	cite that study*		
3. I certify that, for each	h study cited in sup	port of this	application for i	registration that is not an exc	lusive use study;
a. X I am the	original data submit	ter*; or			•
I have ob	tained the written pe	ermission of	f the original da	ta submitter for	, which is
		(1	for multiple che	micals link the companies w	(nsert name of chemical) ho are original data submitters
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b.     I have no	tified in writing the o	companies	linear	for	(nsert name of cnemical)
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Compani	· ·			for	(for multiple
			iginal data sub		et name of chemical) chemical name) that have submitted the
4.   I certify th	at for each study cit	ted in suppo	ort of this applic	ation I am not required to off	fer data compensation or obtain written
permissio	n because all time p	periods for e	exclusive use a	nd data compensation have e	expired.
* A Data Matri	x identifying these s	tudies is att	tached. (Note:	a Data Matrix is not required	d under the cite-all method.)
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	General Offe	er to Pay: The	ereby offer and agre	ee to pay compensation to other per	
Signature	Name	regard to the	approval of this ap	plication, to the extent required.  Title	Date
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## U.S. ENVIRONMENTAL PROTECTION AGENCY Office of Pesticide Programs

DOWELANCO 9330 ZIONSVILLE ROAD INDIANAPOLIS, IN 462681054

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 08/08/96. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your data submittal was found to be partially in compliance with the standards for submission of data contained in PR Notice 86-5, with the exceptions noted A copy of your transmittal bibliography is enclosed, annotated with the Master Record ID's (MRIDs) assigned to each document accepted. Please use these numbers in all future references to these documents. If deficiencies were found which apply to individual accepted studies, they are listed below following the applicable MRID. Any document which has been assigned a MRID has been accepted under PR Notice 86-5. comments related to a MRID appear on this report, they are provided for your information and reference when preparing future submissions. Some individual documents were not acceptable, and all copies are being returned to you for correction for the reasons indicated below. These rejected studies have been assigned separate identification numbers which are annotated on both the enclosed bibliography and the rejected document labels. The rejected studies and their deficiencies are described below.

#### Rejected study [19] :

\* Judging from the pagination of the study, pages..... were omitted from the submitted copy. 111-156

#### Rejected study [44]:

A statement of compliance or non-compliance with the Good Laboratory Practices Standards contained in 40 CFR160 is required for all studies (except range finding studies and supplements to previously submitted studies) submitted to EPA. This statement must appear as page 3 of all studies, and must be signed and dated

by the study sponsor, the study submitter, and the study director. Please see 40 CFR 160.12 for specific quidance.

#### Rejected study [49]:

\* Judging from the pagination of the study, pages..... &6..... were omitted from the submitted copy.

#### Rejected study [60]:

\* Judging from the pagination of the study, pages.....83..... were omitted from the submitted copy.

308/2E August 6, 1996

Mc DowElanco

Document Processing Desk (APPL/PETN)/6(a)(2)<sup>1</sup> Office of Pesticide Programs (7504C)
U. S. Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Attention: Ms. Joanne I. Miller/PM-23 (7505C)

STARANE' F (TECHNICAL) AND STARANE EC (END-USE)

(A.I. FLUROXYPYR METHYLHEPTYL ESTER (MHE))

EPA FILE SYMBOL NUMBERS: 62719-XXX

APPLICATIONS FOR NEW REGISTRATION - SECTION 3

PETITION FOR PERMANENT TOLERANCE- FOR FLUROXYPYR METHYLHEPTYL ESTER (MHE) RESIDUES ON WHEAT. BARLEY AND OATS

DowElanco is respectfully submitting an application for new registration for Starane F herbicide (a technical product) and Starane EC herbicide (an end use product for use on wheat, barley, oats, fallow cropland and non-cropland), which contains fluroxypyr MHE. A petition for permanent tolerance for residues of fluroxypyr MHE and fluroxypyr on wheat, barley and oats accompanies this application.

A check to cover petition fees in the amount of \$61,950.00 (check # 53064046) has been mailed under separate cover letter dated August 6, 1996. A complimentary copy is enclosed in the transmittal document.

DowElanco desires approval of the enclosed permanent tolerance petition and acceptance of the proposed Section 3 registration's for Star 100 F and Starage EC on or before January 31, 1998.

#### Contents of Submission

Volume I (Administrative)

Transmittal document (this letter)
General Summaries for Public Release (63)

Application for Pesticide, EPA Form 8570-1 for Starane F (OPP No. 243062)

Application for Pesticide, EPA Form 8570-1 for Starane EC (OPP No. 249024)

Certification with Respect to Citation of Data for Starane F

Certification with Respect to Citation of Data for Starane EC

Confidential Statement of Formula entitled Starane F (Basic/62719-XXX/06-24-96) (Pages 1 - 2) (2 originals)

Confidential Statement of Formula entitled Starane EC (Basic/62719-XXX/06-10-96) (Pages 1 - 2) (2 originals)

<sup>&</sup>lt;sup>1</sup> Four studies will be flagged to be submitted for 6(a)(2) consideration.

Trademark of DowElanco

Volume 1 (cont'd)

Complimentary Copy: DowElanco letter to EPA dated August 6, 1996, with check # 53064046 to cover Tolerance Fees.

Proposed label entitled Starane F (Technical)
(B2A/Starane F/PropSec3/07-11-96) (Pages 1 - 2) (5 copies)

Proposed label entitled Starane EC (End Use) (B2A/Starane EC/PropSec3/07-29-96) (Pages 1 - 10) (5 copies)

Data Matrix entitled Fluroxypyr MHE dated August 6, 1996 (Pages 1 - 18)(1 copy)

Petition for Permanent Tolerance for Residue of Fluroxypyr MHE and Fluroxypyr on Wheat, Barley and Oats Includes Complimentary Copies of:

Proposed labeling entitled Starane F (2 copies)

(B2A/Starane F/PropSec3/07-11-96) (Pages 1 - 2)

Proposed labeling entitled Starane EC (2 copies)

(B2A/Starane EC/PropSec3/07-29-96) (Pages 1 - 10)

Data Matrix for Fluroxypyr MHE (includes studies previously submitted as well as studies included with this submission dated August 6, 1996) (Pages 1 - 18) (2 copies)

Complimentary Copy (adds supplemental information to the fluroxypyr MHE environmental fate profile):

Aerobic Soil Metabolism of <sup>14</sup>C-Fluroxypyr-MHE Ballatine, Larry G. Ph.D. January 5, 1993 Study ID: ENV92015 GH-C # 3033

Pages: 1-115 (1 copy) (Guideline No. 162-3)

### Product Chemistry (Technical/Starane F)

Volume Guidelin		Contents	
Volume 2 Series 61	44080301	. Series 61: Product Identity and C	Composition of STARANE* Herbicide
	7/00	Paterson, E.S.	July 15, 1996
•		Study ID: GH-C # 4145	(Confidential Attachment pgs 1-38)
		Pages: 1-8	(3 copies)
Volume 3 Series 62	44080302	Series 62: Analysis and Certifica Fluroxypyr-1-methylheptyl Ester (TGAI)	ntion of Preduct Ingredients of Technical Grade of Active Ingredient
•		Ghaoui, L.H.	July 22, 1996
		Study ID: GH-C # 4141	(Confidential Attachment pgs 1-316)
		Pages: 1-77	(3 copies)
Volume 4 Series 63	44080303	Series 63: Physical and Chemica Grade of Active Ingredient, Flury	al Characteristics of the Technical
561163 0.		Ghaoui, L.H. Study ID: GH-C 4093	June 25, 1996
		Pages: 1- 150	(3 copies)

Product Ch	emistry (Sort-Use/Sterums &	<u></u>	
Volume 5 Series 61	44080304	•	Composition of STARANE Herbicide, An lation of Fluroxypyr-1-Methylheptyl
		Paterson, E.S.	July 8, 1996
	·	Study ID: GH-C # 4061 Pages: 1- 8	(Confidential Attachment pgs 1-47) (3 copies)
Volume 6 Series 62	44080305		tion of Product Ingredients of the Endulsifiable Concentrate Containing (1-MHE)
		Ghaoui, L.	July 17, 1996
		Study ID: GH-C # 4033 Pages: 1- 27	(Confidential Attachment pgs 1-4) (3 copies)
Volume 7 Series 63	44080306	Series 63: Determination of Physi XRM-5316, and Emulsifiable Cor Methylheptyl Ester (1-MHE)	ical and Chemical Properties of neentrate Containing Fluroxypyr 1-
		Kinnunen, C.A. Study ID: FOR93081	August 16, 1993
	• .	Pages: 1- 15	(3 copies)

<sup>\*</sup> Trademark of DowElanco

### Wildlife and Aquatic Organisms

Volume Guidelin		Contents	
Volume 8 72-1(a)	44080307	Evaluation of the Acute Toxicity of the Bluegill, Lepomis macrochirus Rick, D.L. et. al Study ID: DECO-ES-3020 Pages: 1-33	Fluroxypyr 1-methylheptyl Ester to Rafinesque March 11, 1996 (3 ccysies)
Volume 9 72-3(a)	44080308	Fluroxypyr 1-Methylheptyl Ester: Alinnow, Cyprinodon variegatus Boeri, R.L. et.al Study ID: 707-DO Pages: 1- 24	January 15, 1996 DECO-ES-2961 (3 copies)
Volume 10 72-3 (a)	44080309	Fluroxypyr: Acute Toxicity to the S Boeri, R.L. et. al Study ID: 199-DO (ES-2644) Pages: 1-26 (3 copies)	February 4, 1994 DECO-ES-2644 (Amended date June 8, 1994)
Volume 11 72-3 (b)	44080310	Fluroxypyr 1-Methytheptyl fister: 7 Deposition Test Boeri, R.L. et. al Study ID: 646-DO Pages: 1-28	January 12, 1996 DECO-ES-2925 (3 copies)
Volume 12 72-3(b)	44080311	Fluroxypyr: Acute Flow-through M Boeri, R.L. et.al Study ID: 198-DO (ES-2645) Pages: 1- 25	February 3, 1994 DECO-ES-2645 (3 copies)
Volume 13 72-3(c)	44080312	Fluroxypyr: Acute Toxicity to the C Boeri, R.L. et. äl Study ID: 197-DO (ES-2643) Pages: 1- 24	February 14, 1994 DECO-ES-2643 (3 copies)
Volume 14 72-3(c)	44880313	Fluronypyr 1-Methylheptyl Ester: A Palaemonetes pugio Boeri, R.L. et. al Study ID: 706-DO Pages: 1- 24 (3 copies)	December 7, 1995 DECO-ES-2962 (Amended January 12, 1996)

Ms. Joanne I. Miller/PM-23 (7505C) APPLICATIONS FOR NEW REGISTRATION -

SECTION 3 FOR STARANE F (TECHNICAL) AND STARALLE EC (EMD-USE)

Page 5

1

Wildlife and Aquatic Organisms (continued)

Volume No. Guideline No. MRID No.

Contents

Volume 15 44080314 72-4

Evaluation of the Chronic Toxicity of Fluroxypyr 1-Methylheptyl Ester to the Daphnid, Daphnia magna STRAUS

Kirk, H.D. et.al

July 15, 1996

Study ID: DECO-ES-3079

Pages: 1-78

(3 copies)

44080315 Volume 16 Ν/A

A Review of the Toxicity of Fluroxypyr Herbicide to Fish and Wildhife

July 31, 1996

Maves, M. A. Study ID: DECO-ES-3150

Pages: 1-50

(3 copies)

Mammalian Toxicology

Volume No. Guideline No. MRID No.

Contents

Volume 17

82-1

440803/6

Fluroxypyr: 13-Week Dietary Toxicity Study and 4-Week Recovery Study in Fischer 344 Rais Place 24, 11 72

Grandsean, M. et.al.

Study ID: K-129976-007

Pagest 1- 238

(3 copies)

44080317 Volume 18

83-2

Fluroxypyr: 18-Month Dietary and Oncogenicity Study in CD-1 Mice

Cossc, P.F. et.al

Study ID: K-129976-004

Pages: 1-994

July 20, 1993

(3 copies)

REJECTED (19) Volume 19

83-3

Ester Schroeder, R.E.

May 3, 1994

Study ID: 93-4052

(K-137992-007)

Pages: 1-461

(3 copies) (No FOI pages)

Volume 20

N/A

44080318

A Range-Finding Study to Evaluate the Developmental Toxicity Study of Fluroxypyr Methylheptyl Ester in the Rat

A Developmental Toxicity Study in Rats w/Fluroxypyr Methylheptyl

Schroeder, R. E.

May 3, 1994

Study ID: 93-4051

(K-137992-006)

Pages: 1-212

(3 copies)(No FOI pages)

#### Mammalian Toxicology (continued)

Volume No. Guideline No. MRID No.

Contents

Volume 21

44080319 83-3(b)

Fluroxypyr Methylheptyl Ester: Oral Gavage Teratology Study in New

Zealand White Rabbits

Liberacki, A. B. et. al

May 2, 1996

Study ID: K-137992-013

Pages: 1- 239

(3 copies)

44080320

-- N/A

Fluroxypyr Methylheptyl Ester: Oral Gavage Teratology Probe Study in

New Zealand White Rabbits

Liberacki, A.B. et. al.

May 2, 1996

Study ID: K-137992-012

Pages: 1-85

(3 copies)

Volume 23 (1-2) 44080321 83-4

6(a)(2) consideration

Fluroxypyr: Two Generation Dietary Reproductive Toxicity Study in Sprague-Dawley Rats

Vedula, U. et.al

Study ID: K-129976-012

Pages: 1-996

(3 copies)

June 19, 1996

Velume 24 (1-3) 44020322 \$3-5

Pluroxypyr: Two Year Liet. ... Chronic Toxicity Oncogenitaty hady in

Fischer 344 Rats - Final Report

Quast, J.F. et.al

June 15, 1995

Study ID: K-129976-008(1)

Pages: 1-1553.

(3 copies)

Volume 25 84-2

44080323

Mutagenicity Test with Fluroxypyr Methylheptyl Ester in the

Salmonella -Escherichia Coli/Mammalian-Microsome Reverse Mutation

Assay Preincubation Method with a Confirmatory Assay

Lawlor, T. E.

December 28, 1995

Study ID: 16848-0-422R

(K-129976-008)

Pages: 1-38

#### Mammalian Toxicology (continued)

Volume No. MRID No. Contents Guideline No. Evaluation of Fluroxypyr Methylheptyl Ester in the Chinese Hamster Volume 26 44080324 84-2 Ovary Cell/Hypoxanthine-Guanine-Phosphoribosyl Transferase (CHO/HGPRT) Forward Mutation Assay Linscombe, V.A. et.al January 23, 1996 Study ID: K-137992-009 Pages: 1-39 (3 copies) 4408032 Voiume 27 Evaluation of Fluroxypyr Methylheptyl Ester in an In Vitro Chromosomal Aberration Assay Utilizing Rat Evaplacettes Linscombe, A.V. et. al. January 16, 1996 Study ID: K-137992-010 - Pages: 1-42 (3 copies) 44080326 Volume 28 Evaluation of Fluroxypyr Methylheptyl Ester in the Mouse Bone 84-2 Marrow Micronucleus Test Lick, S.J. et.al January 15, 1995 Study ID: K-137992-011 Pages: 1- 52 (3 copies) 44080327 Volume 29 Fluroxypyr Methylheptyl Ester (Fluroxypyr MHE) and Methylheptanoi. 85-1 Metabelism in Male Fischer 344 Rats Dem stadiski, J.Y. et al. June 3, 150 % Study ID: K-137992-014 Pages: 1-78 (3 copies) 44080328 Volume 30 A Review of the Mammalian Toxicity of Fluroxypyr and Fluroxypyr 1-Methylheptyl Ester Eisenbrandt, D. L. July 31, 1996

#### Mammalian Toxicology (End-Use/Starane EC)

Volume No. MRID Guideline No.	No. Contents		
Volume 31 81-1 440803	XRM-5316: Acute Oral	XRM-5316: Acute Oral Toxicity Study in Fischer 344 Rats	
7 7000	Cosse, P.F. et.al Study ID: M-005316-00	November 20, 1992 DIA	
	Pages: 1- 51	(3 copies)	

Pages: 1- 56

Study ID: T2.02-204-000-001

(3 copics)

#### Mammalian Toxicology (End-Use/Starane EC) (continued)

Volume Guideline		Contents .	
Volume 32 81-2	44080330	XRM-5316: Acute Dermal Toxicity Study in New Zealand White Rabbits	
		Cosse, P.F. et.al Study ID: M-005316-001D	November 20, 1992
		Pages: 1- 29	(3 copies)
Volume,33 81-3	44080331	XRM-5316: Acute Inhalation Toxicity Study with Fischer 344 Rats	
		Bookman, M.J. et.al Study ID: M-005316-002	February 18, 1993
		Pages: 1- 35	(3 copies)
Volume 34 81-4	44080332	XRM-5316: Primary Eye Irritation Study in New Zealand Rabbits	
		Cosse, P.F. <i>et.al</i> Study ID: M1-005316-001C	November 20, 1992
		Pages: 1- 16	(3 copies)
Velume 35 81-5	440 90333	XRM-5316: Primary Dermal Irritation Study in New Zealand White Robbis	
		Cosse, P.F. <i>et.al</i> Study ID: M-005316-001B	November 20, 1992
		Pages: 1- 15	(3 copies)
Volume 36 81-6	44080334	XRM-5316: Dermal Sensitization Potential in the Hartley Albino Guinea Pig	
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6(a)(2) consideration		Milazzo, D.P. et.al Study ID: ES-3073	June 4, 1996
		Pages: 1- 55	(3 copies)
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		Kirk, H.D. et.al	June 4, 1996
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#### Residue Chemistry

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The Magnitude of Residue of Fluroxypyr in Oats Following

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Phillips, A.M. et.al.

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Fluroxypyr in or on Barley, Oats and Wheat: Sections E, F and G of the

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Hamburg, A. W

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Olberding, E. L.

August 2, 1996

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If you require further information, please contact me at the number listed below or Ms. Joyce Armstrong, Registration Assistant for this product, at (317) 337-4657.

Sincerely,

Robert F. Bischoff

Product Registration Manager U.S. Regulatory, Toxicology and

**Environmental Chemistry** 

(317) 337-4686

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RFB/car

**Enclosures** 

(Data submitted 8/6/96 are listed in BOLD)

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Product (	ChemistryTGAI						
61-1	Product Identification and Disclosure o Ingredients	Series 61: Product Identity and Composition of STARANE* F Herbicide	Vergrugge	11/15/91	12/9/91	42137322	
61	Product Identification and Disclosure of Ingredients	Series 61: Product Identity and Composition of STARANE* F Herbicide	Paterson	7/15/96	8/6/96	GH-C 4145	·
62-1	Analytical and Certification of Limits	Series 62: Analysis and Certification of Product Ingredients for Fluroxypyr 1-MHE	Hamilton Bhuva	11/18/91	12/9/91	42137323	
62	Analytical and Certification of Limits	Series 62: Analysis and Certification of Product Ingredients of Fluroxypyr-1-methylheptyl Ester Technical Grade of Active Ingredient (TGA1)	Ghaoui	7/22/96	8/6/96	GH-C 4141	
63	Physical and Chemical Characteristics	Series 63: Physical and Chemical Characteristics of Fluroxypyr 1-MHE	Hamilton Knowles	11/18/91	12/9/91	42137324	Not applicable 63-6 (Boiling Pt), 63-12 (pH), 63-15 (Flam.), 63-18 (Viscosity), 63-19 (Misc), 63-21 (Dielectrie). Not applicable due to low water solubility 63-10 (Dissociation). To be submitted after registration 63-17 (SS) and 63-20 (Corrosion).
63	Physical and Chemical Characteristics	Series 63: Physical and Chemical Characteristics of the Technical Grade of Active Ingredient, Fluroxypyr-1-methylheptyl Ester	Ghaoui	6/25/96	.8/6/96	GH-C 4093	

RECD EPA/SPP/DPD1

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Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Wildlife a	and Aquatic Organisms	TGAI					
71-1(a)	Acute Avian Oral Toxicity (LD50) in Mallard Duck (Ester)	The Acute Oral Toxicity (LD50) of DOWCO 433 to the Mallard Duck	Roberts Phillips	6/10/83	5/21/87	40244516	Generally meets requirements per EPA on 9/29/88
71-1(a)	Acute Avian Oral Toxicity (LD50) in Mallard Duck (Acid)	The Acute Oral Toxicity (LD50) of DOWCO 433 Acid to the Mallard Duck	Roberts Phillips	3/22/84	5/21/87	40244514	Generally meets requirements per EPA on 9/29/88
71-1(a)	Acute Avian Oral Toxicity (LD50) in Bobwhite Quail (Ester)	The Acute Oral Toxicity (LD50) of DOWCO 433 Ester to the Bobwhite Quail	Roberts Phillips	3/22/84	5/21/87	40244546	Generally meets requirements per EPA on 9/29/88
71-1(a)	Acute Avian Oral Toxicity (LD50) in Bobwhite Quail (Acid)	The Acute Oral Toxicity (LD50) of DOWCO 433 Acid to the Bobwhite Quail	Roberts Phillips	3/23/84	5/21/87	40244515	Fulfills the requirements per EPA on 9/29/88
71-2(a)	Acute Avian Dietary Toxicity (LC50) in Bobwhite Quail (Ester)	The Subacute Dietary Toxicity (LC50) of DOWCO 433 Ester to the Bobwhite Quail	Roberts Phillips	11/16/83	5/21/87	40244517	Fulfills the requirements per EPA on 9/29/88
71-2(a)	Acute Avian Dietary Toxicity (LC50) in Bobwhite Quail (Acid)	The Subacute Dietary Toxicity (LC50) of DOWCO 433 Acid to the Bobwhite Quail	Roberts Phillips	11/15/83	5/21/87	40244547	Fulfills the requirements per EPA on 9/29/88
71-2(b)	Acute Avian Dietary Toxicity (LC50) in Mallard Duck (Ester)	Fluroxypyr 1-methylheptyl ester: A Dietary LC50 Study with the Mallard	Grimes Jaber	5/13/88	12/9/91	42137301	Core status per EPA on 7/25/94
71-2(b)	Acute Avian Dietary Toxicity (LC50) in Mallard Duck (Acid)	Fluroxypyr: A Dietary LC50 Study with the Mallard	Grimes	8/2/91	12/9/91	42137302	Core status per EPA on 7/25/94
71-4(a)	Avian Reproductive Toxicity in the Bobwhite Quail (Ester)	Fluro: /pyr 1-Methylheptyl Ester Herbicide, ((4-Amino-3,5-dichloro-6-fluoro-2-pyridinyl)oxy)acetic acid, 1-methylheptyl ester: A One Generation Reproduction Study with the Bobwhite (Colinus virginianus)	Beavers Hawrot Jaber	11/29/89	1 <i>2/9/</i> 91	42137303	Core status per EPA on 7/25/94
71-4(b)	Avian Reproductive Toxicity in the Mallard Duck (Ester)	Fluroxypyr 1-Methylheptyl Ester Herbicide. ((4-Amino-3,5-dichloro-6-fluoro-2-pyridinyl)oxy)acetic acid, 1-methylheptyl ester: A One Generation Reproduction Study with the Mallard (Anas platyrhynchus)	Beavers Hoxter Nichols Hawrot Jaber	12/6/89	12/19/91	42137304	Core status per EPA on 7/25/94
72-1(a)	Fish Toxicity in Bluegill Sunfish (Ester)	Fluroxypyr 1-Methylheptyl Ester: Evaluation of the Toxicity to the Bluegill, Lepomis macrochirus Rafinesque	Dill Bartlett	6/5/89	12/19/91	42137305	Invalid per EPA on 7/25/94
72-1(a)	Fish Toxicity in Bluegill Sunfish (Acid)	Fluroxypyr: Evaluation of the Acute Toxicity to the Bluegill, (Lepomis macrochirus) Rafinesque	Weinberg Richardson Rick Piasecki	9/17/91	12/19/91	42137306	Core status per EPA on 7/25/94

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Wildlife (	and Aquatic Organisms	TGAI (Cont.)					
72-1(a)	Fish Toxicity in Bluegill (Ester)	Evaluation of the Acute Toxicity of Fluroxypyr 1- Methylheptyl Ester to the Bluegill, Lepomis Macrochirus Rafinesque	Rick	3/11/96	8/6/96	DECO-ES-3020	
72-1(c)	Fish Toxicity in Rainbow Trout (Acid)	The Acute Toxicity of DOWCO 433 Acid to Rainbov Trout	Willis	5/16/84	5/21/87	40244518	Fulfills the requirements per EPA on 9/29/88.
72-1(c)	Fish Toxicity in Rainbow Trout (Ester)	Fluroxypyr, 1-Methylheptyl Ester: Evaluation of the Acute Toxicity to the Rainbow Trout,  Oncorhynchus mykiss Walbaum	Weinberg Richardson Dick Piasecki	9/17/91	12/19/91	42137307	Core status per EPA on 7/25/94.
72-2(a)	Invertebrate Toxicity Freshwater LC50 (Daphnia Preferred) (Acid)	The Acute Toxicity of DOWCO 433 Acid to Daphnia Magna	Jones	4/18/84	5/21/87	40244524	Fulfills the requirements per EPA on 9/29/88
72-2(a)	Invertebrate Toxicity Freshwater LC50 (Daphnia Preferred) (Ester)	Fluroxypyr, 1-Methylheptyl Ester: Evaluation of the Acute Toxicity to the Water Flea, <i>Daphnia magna</i> Straus.	Weinberg Milazzo Servinski Rick	10/16/91	12/19/91	42137308	Core status per EPA on 7/25/94.
72-3	Acute LC50 estuarine and marine organisms (Acid)	Fluroxypyr: Acute Toxicity to the Silverside, Menidia beryllina	Boeri	2/4/94 Amended 6/8/94	8/6/96	199-DO (ES-2644)	
72-3(a)	Toxicity to Estuarine and Marine Organisms (in fish) (Ester)	Flurox vpyr 1, MHE: Acute Toxcity to Atlantic Silversides (Menidia menidia) Under Flow-through Conditions	Manning	8/26/88	12/19/91	42137309	Supplemental per EPA on 7/25/94
72-3(a)	Toxicity to Estuarine and Marine Organisms in Fish (Ester)	Fluroxypyr 1-Methylheptyl Ester: Acute Toxicity to the Sheepshead Minnow, Cyprindon variegatus	Kowalski	1/15/96	8/6/96	707-DO (DECO-ES-2961)	
72-3(b)	Toxicity to Estuarine and Marine Organisms (in mollusks) (Ester)	Fluroxypyr 1, MHE: Shell Growth with the Eastern Oyster (Crassostrea virginca)	Manning	8/26/88	12/19/91	42137310	Invalid per EPA on 7/25/94
72-3(b)	Toxicity to Estuarine and Marine Organisms in Mollusks (Ester)	Fluroxypyr 1-Methylheptyl Ester: Acute Flow- Through Mollusk Shell Deposition Test	Kowalski	1/12/96	8/6/96	646-DO (DECO-ES-2925)	
72-3(b)	Toxicity to Estuarine and Marine Organisms in Mollusks (Acid)	Fluroxypyr: Acute Flow-Through Mollusc Shell Deposition Test	Boeri	2/3/94	8/6/96	198-DO (ES-2645)	·
72-3(c)	Toxicity to Estuarine and Marine Organisms (in shrimp) (Ester)	Fluroxypyr 1, MHE: Acute Toxicity to Pink Shrimp (Penacus duorarum) Under Flow-Through Conditions	Manning	8/26/88	12/19/91	42137311	Supplemental per EPA on 7/25/94.

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Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Wildlife a	and Aquatic Organisms	TGAI (Cont.)					
72-3(c)	Acute LC50 estuarine and marine organisms in shrimp (Acid)	Fluroxypyr: Acute Toxicity to the Grass Shrimp, Palaemonetes pugio	Boeri	2/14/94	8/6/96	197-DO (DECO-ES-2643)	
72-3(c)	Marine Organisms in Shrimp	Fluroxypyr 1-Methylheptyl Ester: Acute Toxicity to the Grass Shrimp, Palaemonetes pugio	Kowalski	12/7/95	8/6/96	706-DO (DECO-ES-2962)	
72-4	Fish early life stage and aquatic	Evaluation of the Chronic Toxicity of Fluroxypyr 1-Methylheptyl Ester to the Daphnid, <i>Daphnia magna</i> Straus	Kirk, II.D.	7/15/96	8/6/96	DECO-ES-3079	
72-6	Accumulation in Fish and Aquatic Organisim Accumulation Study	(See Environmental Fate 165-4)			8/6/96		
N/A	1 k cotovicology Summary	A Review of the Toxicity of Fluroxypyr Herbicide to Fish and Wildlife	Mayes, M.	7/31/96	8/6/96	DECO-ES-3150	

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Conuments
Mammal	lian ToxicologyTGAI						
81-1	Acute Oral Toxicity in the Rat	DOWCO 433 1-Methylheptyl Ester: Acute Oral Toxicity Study (LD50) in the Rat	Jones	11/1/82	5/21/87	40354005	Tox Category IV. Guideline status per EPA on 5/4/88.
81-2	Acute Dermal Toxicity .	DOWCO 433 1-Methylheptyl Ester: Acute Dermal Median Lethal Dose (LD50) in the Rat	Jones	11/1/82	5/21/87	40354006	Tox Category III. Guideline status per EPA on 5/4/88.
81-3	Acute Inhalation Toxicity Study in the Rat	DOWCO 433: Acute Inhalation Toxicity in Rats: 4- Hour Exposure	Hardy Jackson	11/28/84	5/21/87	40244504	Tox Category III. Minimum status per EPA on 5/4/88.
81-4	Primary Eye Irritation in the Rabbit	DOWCO 433 1-Methylheptyl Ester: Eye Irritation Study in the Rabbit	Jones	11/1/82	5/21/87	40354007	Tox Category III. Minimum status per EPA on 5/4/88.
81-5	Primary Dermal Irritation	DOWCO 433 1-Methylheptyl Ester: A Primary Skin Irritation and Corrosivity Study in the Rabbit	Jones	. 11/1/82	5/21/87	40354008	Tox Category IV. Minimum status per EPA on 5/4/88.
81-6	Dermal Sensitization	Fluroxypyr Methylheptyl Ester: Dermal Sensitization Potential in the Hartley Albino Guinea Pig	Berdasco	9/20/90	12/9/91	42137335	Core minimum per EPA on 4/26/93
82-1(a)	90-Day Feeding Study-Rat (Acid)	Sub-Chronic (90-Day) Oral Toxicity Study, Including a Recovery Study, with DOWCO 433 Acid in Rats	Jonker Til Falke Kuijpers	7/2/87	12/9/91	42164502	Core minimum status per EPA on 7/21/92.
82-1(a)	90-Day Feeding Study-Rat (Ester)	Fluroxypry Methylheptyl Ester: 13-Week Dietary Toxicity Study and 5-Week Recovery Study in Fischer 344 Rats	Cosse Vedula Crissman	1/15/91	12/9/91	42137336	Core minimum status per EPA on 4/26/93
82-1(a)	90-Day Feeding Study-Mouse (Acid)	Fluroxypyr: 13-Week Oral Subchronic Toxicity Study in Mice	Shirasu Yoshido Ebino Tsuda Inui Goto	10/1/88	12/9/91	42137337	Core minimum status per EPA on 7/21/92.
82-1	90-Day Feeding studiesrodent and nonrodent (Acid)	Fluroxypyr: 13-Week Dietary Toxicity Study and 4-Week Recovery Study in Fischer 344 Rats	Grandjean	6/24/92	8/6/96	K-129976-007	
82-2	21-Day Dermal-Rabbit (Ester)	Fluroxypyr Methylheptyl Ester: Dermal Probe Study and 21-Day Dermal Toxicicty Study in New Zealand White Rabbits	Cosse Crissman Vedula	9/11/91	12/9/91	42137338	Core minimum status per EPA on 7/21/92.
83-1(a)	Chronic Feeding Study in the Rat (Acid)	Two-Year Chronic Oral Toxicity and Carcinogencity Study with DOWCO 433 Acid in Rats	Til Falke Bosland	1/16/85	5/21/87	40244506	Core supplementary status per EPA on 7/21/92.

(Data submitted 8/6/96 are listed in BOLD)

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Mammal	ian ToxicologyTGAI	(Cont.)					
83-1(a)	Chronic Feeding Study in the Rat (Acid)	Fluroxypyr: Two-Year Chronic Dietary Toxicity/Oncogenicity Study in Fischer 344 Rats - Interim (6 Month) Report	Bond	10/19/92	11/3/92	42540902	
83-1(a)	Chronic Feeding Study in the Rat (Addendum) (Acid)	ADDENDUM: Two-Year Chronic Oral Toxicity and Carcinogenicity Study with DOWCO 433 Acid in Rats	Til Falke Bosland	1/16/85	12/9/91	42137339	Core supplementary status per EPA on 7/21/92.
83-1(b)	Chronic Feeding Study in the Dog (Acid)	12-Month Toxicity Study in Beagle Dogs by Dietary Administration of DOWCO 433	Kinkel	12/12/84	5/21/87	40244507	Core minimum status per EPA on 7/21/92.
83-1(b)	Chronic Feeding Study in the Dog (Addendum) (Acid)	Four-Weeks Range Finding Study in Beagle Dogs by Dietary Administration of DOWCO 433	Ehard Kinkel Raasch Knoell	8/1/83	12/9/91	42137340	Acceptable study per EPA on 7/21/92.
83-2(a)	Oncogenicity Study in the Rat (Acid)	Two-Year Chronic Oral Toxicity and Carcinogencity Study with DOWCO 433 Acid in Rats	Til Falke Bosland	1/16/85	5/21/87	40244506	Core supplementary status per EPA on 7/21/92.
83-2(a)	Oncogenicity Study in the Rat (Acid)	Fluroxypyr: Two-Year Chronic Dietary Toxicity/Oncogenicity Study in Fischer 344 Rats - Interim (6 Month) Report	Bond	10/19/92	11/3/92	42540902	·
83-2(a)	Oncogenicity Study in the Rat (Addendum) (Acid)	ADDENDUM: Two-Year Chronic Oral Toxicity and Carcinogenicity Study with DOWCO 433 Acid in Rats	Til Falke Bosland	1/16/85	12/9/91	42137339	Core supplementary status per EPA on 7/21/92.
83-2	Oncogenicity study in the mouse (Acid)	Fluroxypyr: 18-Month Dietary Oncogenicity Study in CD-1 Mice	Cosse	7/20/93	8/6/96	K-129976-004	
83-3(a)	Teratogenicity in the Rat (Acid)	Effect of DOWCO 433 on Pregnancy of the Rat	Bottomley Mayfield	3/31/83	5/21/87	40244509	Guideline status per EPA on 5/4/88.
83-3(b)	Teratogenicity in the Rabbit (Acid)	DOWCO 433: Effects of Oral Administration Upon Pregnance in the Rabbit	Tesh Ross	2/2/84	5/21/87	40354013	Core minimum status per EPA on 7/21/92.
83-3(b)	Teratogenicity in the Rabbit (Addendum) (Acid)	ADDENDUM: DOWCO 433: Effects of Oral Administration Upon Pregnanacy in the Rabbit	Tesh Ross Wightman	10/27/88	12/9/91	42137341	Core minimum status per EPA on 7/21/92.
N/A	Range-Finding (Probe) Study (Ester)	A Range-Finding Study to Evaluate the Developmental Toxicity Study of Fluroxypyr Methylheptyl Ester in the Rat	Schroeder	5/3/94	8/6/96	93-4051 (K-137992-006)	
83-3	Teratogenicity in the Rat (Ester)	A Developmental Toxicity Study in Rats w/ Fluroxypyr Methylheptyl Ester	Schroeder	5/3/94	8/6/96	93-4052 (K-137992-007)	

\*Trademark of DowElanco m:\FluroxypyrSect3.xls Prepared by: J. Armstrong DowElanco Submitted by: Robert F. Bischoff Matrix Submitted to EPA: 8/6/96

# Fluroxypyr MHE Matrix (Data submitted 8/6/96 are listed in BOLD)

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission :	MRID Number or DowElanco Study ID Number	Comments
Mammal	ian ToxicologyTGAI	(Cont.)					
N/A	Probe Study	Fluroxypyr Methylheptyl Ester: Oral Gavage Teratology Probe Study in New Zealand White Rabbits	Liberacki	5/2/96	8/6/96	K-137992-012	
83-3(b)	Teratogenicity in the Rabbit	Fluroxypyr Methylheptyl Ester: Oral Gavage Teratology Study in New Zealand White Rabbits	Liberacki	5/2/96	8/6/96	K137992-013	
83-4	2-Generation Reproduction Study in the Rat (Acid)	Oral Multigeneration Reproduction Study with DOWCO 433 Acid	Koeter Van Marwijk Bosland	3/1/84	5/21/87	40244510	Core supplemetary status per EPA on 7/21/92.
83-4	2-Generation Reproduction Study in the Rat (Addendum)(Acid)	ADDENDUM: Oral Multigeneration Reproduction Study with DOWCO 433 Acid in Rats	Koeter van Marwijk Bosland	3/21/84	12/9/91 ·	42137342	Core supplemetary status per EPA on 7/21/92.
83-4	2-Generation Reproduction Study in the Rat (Acid)	Fluroxypyr: Two-Generation Dietary Reproduction Toxicity Study in Sprague-Dawley Rats	Vedula	6/19/96	8/6/96	К-129976-012	
83-5	Chronic Feeding/Oncogenicity in the Rat (Acid)	Fluroxypyr: Two-Year Dietary Chronic Toxicity/Oncogenicity Study in Fischer 344 Rats - Final Report	Quast	6/15/95	8/6/96	K-129976-008 <del>(1)</del>	
84-2	Ames Test(Acid)	Ames Metabolic Activation Test to Assess to Potential Mutagenic Effect of DOWCO 433	Hossack Richold	1/1/79	5/21/87	40354014	Acceptable study per EPA on 5/4/88.
84-2	Cytogenetics in Vitro (Acid)	Dow433: Cytogenetic Study in Chinese Hamsters	Holmstrom McGregor	4/1/83	5/21/87	40354017	Unacceptable study per EPA on 5/4/88.

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Mammal	ian ToxicologyTGAI	(Cont.)					
84-2	CHO/HGPRT(Acid)	An Investigation into the Possible Induction of Point Mutations at the HGPRT-Locus of Chinese Hamster Ovary Cells by DOWCO 433	Davis	7/11/83	5/21/87	40244511	Acceptable study per EPA on 5/4/88.
84-2	Mouse Lymphoma(Acid)	DOWCO 433: Assessment of Mutagenic Activity in Mouse Lymphoma	McGregor Riach	3/1/83	5/21/87	40354015	Acceptable study per EPA on 5/4/88.
84-2(b)	Structural Chromosome AberrationChromosomal Aberrations CHO Cells (Acid)	DOWCO 433: Chromosomal Aberrations Assay with Chinese Hamster Ovary Cells in Vitro	Holmstrom McGregor	3/1/83	5/21/87	40354016	Acceptable study per EPA on 5/4/88.
84-2	Gene Mutation (Ester)	Evaluation of Fluroxypyr Methylheptyl Ester in the Chinese Hamster Ovary Cell/Hypoxanthine-Guanine-Phosphoribosyl Transerase (CHO/HGPRT) Forward Mutation Assay	Linscombe	1/23/96	8/6/96	K-137992-009	
84-2	Gene Mutation (Ester)	Evaluation of Fluroxypyr Methylheptyl Ester in an In Vitro Chromosomal Aberration Assay Utilizing Rat Lymphocytes	Linscombe	1/16/96	8/6/96	K137992-010	
84-2	Gene Mutation (Ester)	Evaluation of Fluroxypyr Methylheptyl Ester in The Mouse Bone Marrow Micronucleus Test	Gollapudi	1/15/96	8/6/96	K-137992-011	
84-2	Gene Mutation (Ester)	Mutagencity Test with Fluroxypyr Methylheptyl Ester in the Salmonella - Escherichia Coli/Mammalian-Microsome reverse mutation assay preincubation method with a confirmatory Assay	Lawlor	12/28/95	8/6/96	16848-0-422R (K-129976-008)	
84-4	Other Genotoxic Effects Unscheduled DNA Synthesis (Acid)	DOWCO 433: Assessment of Genotoxicity by Unscheduled DNA Synthesis in Human Embryonic Cells	McGregor Riach	2/1/83	5/21/87	40354018	Acceptable study per EPA on 5/4/88.
85-1	General MetabolismRat (Acid)	DOWCO 433 Pharmacokinetic Study in Male Wistar Rats	Veenstra Hermann	6/1/83	5/21/87	40244512	Acceptable study per EPA on 5/4/88.
85-1	General MetabolismRat (Ester)	The Biokinetics and Metabolism of 14C-DOWCO 433 Methylheptyl Ester in Rats	Hawkins Kirkpatrick	1/5/81	5/21/87	40244513	Supplementary study per EPA on 5/4/88.

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Mammal	ian ToxicologyTGAI	(Cont.)					
85-1		ADDENDUM: 'The Biokinetics and Metabolism of 14C-DOWCO 433 Methylheptyl Ester in Rats	Hawkins Kirkpatrick	2/13/90	12/9/91	42137343	Acceptable study but does not meet guideline requirement per EPA on 7/21/92.
85-1	(Ester)	Fluroxypyr Methylheptyl Ester (Fluroxypyr MHE) and Methylheptannol: Metabolism in Male Fischer 344 Rats	Domoradzki	6/3/96	8/6/96	K-137992-014	
N/A	Toxicology Summary	A Review of the Mammalian Toxicity of Fluroxypyr and Fluroxypyr 1-Methylheptyl Ester	Eisenbrandt	7/31/96	8/6/96	T2.02-204-000-001	

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Plant Pro	tectionTGAI						
122-2 and 123-2	Tier I: Aquatic Plant Growth Tier II: Aquatic Plant Growth (Ester)	Fluroxypyr 1-Methylheptyl Ester: The Toxicity To Skeletonema costatum	Alexander	5/31/96	8/6/96	10-04-1 (DECO-ES-3131)	·
123-1	Tier II: Non-Target Terrestrial Plants (Ester)	Evaluating the Effects of Fluroxypyr-MHE on the Seedling Emergence and Vegetative Vigor of Non-Target Terrestrial Plants	Schwab	5/7/96	8/6/96	RES95175 (ABC Lab #42838) (GH-C 4053)	
123-2	Aquatic Plant Growth (Ester)	The Toxicity of Fluroxypyr 1-Methylheptyl Ester to Selenastrum capricornutum	Hughes Alexander	10/9/91	12/9/91	42137312	Supplemental per EPA on 7/25/94.
123-2	Aquatic Plant Growth (Acid)	The Five-Day Toxicity of Fluroxypyr (DOWCO 433) to Selenastrum capricornutum Printz, A Freshwater Green Algae	Cowgill Milazzo Murphy	1/22/88	12/9/91	42164501	Invalid per EPA on 7/25/94.
123-2		Fluroxypyr 1-Methylheptyl Ester: The Toxicity to the Blue-Green Alga, Anabaena flos-aquae	Milazzo	6/4/96	8/6/96	ES-3073	
123-2	Tier II: Non-Target Terrestrial Plants (Ester)	Fluroxypyr 1-Methylheptyl Ester: The Toxicity to the Aquatic Plant Duckweed, Lemma gibba L G-3	Milazzo	6/4/96	8/6/96	ES-3074	
123-2	Tier II: Aquatic Plant Growth (Ester)	Fluroxypyr 1-Methylheptyl Ester: The Toxicity to the Freshwater Diatom, Navicula pelliculosa	Milazzo	6/4/96	8/6/96	ES-3075	
123-2	Tier II: Aquatic Plant Growth (Ester)	Fluroxypyr 1-Methylheptyl Ester: The Toxicity to the Freshwater Green Alga, Selanastrum capricornutum Printz	Milazzo	6/4/96	8/6/96	ES-3076	
N/A	Evaluation of Phytotoxicity	Evaluation of the Phytotoxicity of 4-Amino-3,5-Dichloro-6-Fluoro-2- Methoxypyridine to the Green Algae, Selenastrum capricornutum Printz	Kirk	10/6/95	8/6/96	DECO-ES-3029	
N/A	Evaluation of Phytotoxicity	Phytotoxicity of Fluroxypyr MHE and its Metabolites Fluroxypyr, Methoxypyridine, and Pyridinol to Non-Target Terrestrial Plants	Wright	11/20/95	8/6/96	GH-C 3859	

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
	Honey Bee Acute Contact (LD50)	Fluroxypyr, I-MHE: An Acute Contact Toxicity Study with the Honey Bee	Lynn Hoxter	8/20/91	12/9/91	42137313	Core status per EPA on 7/25/94.
141-1	1	Fluroxypyr: An Acute Contact Toxicity Study with the Honey Bee	Lynn Hoster	8/20/91	12/9/91	42137314	Core status per EPA on 7/25/94.

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Environn	nental FateTGAI						
N/A	Summary	A Review of the Environmental Fate of Fluroxypyr- I-Methylheptyl Ester in, Soil	Lehmann	10/10/90	12/9/91	42137315	
161-1	Hydrolysis	The Hydrolysis of Fluroxypyr-MHE in Dilute Aqueous Solution	Lehmann	5/29/87	5/21/87	40244539	Accepted by EPA on 11/30/87.
161-1	Hydrolysis	Formation of Fluroxypyr from Fluroxypyr-MHE by Soil Catalysis	Lehmann	6/13/88	12/9/91	42137316	
161-2		The Aqueous Photolysis of Fluroxypyr Methylheptył Ester and Fluroxypyr (Acid) in Natural Sunlight	Cleveland	7/27/92	8/6/96	ENV91079 (GH-C 2758)	
161-3	I Dhatadageadation: The Soil	Soil Photolysis of Fluroxypyr 1-Methylheptyl Ester in Natural Sunlight	Batzer	3/3/92 Amended 7/31/96	8/6/96	ENV91080 (GH-C 2717R)	
162-1	Aerobic Soil Metabolism Study	Aerobic Soil Metabolism of Fluroxypyr-MHE	Lehmann	1/30/89	12/9/91	42137317	
162-1	Aerobic Soil Metabolism Study	A Review of 2-Octanol, Hydrolysis Product of Fluroxypyr-1-Methylheptyl Ester	Lehmann	8/13/91	.12/9/91	42137318	
162-1	Aerobic Soil Metabolism Study	Response to EPA Review of Fluroxypyr EUP Submission	Cleveland	3/26/93	4/7/93	42730001	
162-1	Acrobic Soil Metabolism Study	Acrobic Soil Metabolism of 14c-Fluroxypyr- MHE	Ballantine	4/5/93	8/6/96	ENV92015 (GH-C 3026)	Supplemental information submitted as a Complementary Copy.
162-3	Anaerobic Aquatic Soil Metabolism Study	Anacrobic Aquatic Metabolism of Fluroxypyr Methylheptyl Ester	Cleveland	6/24/93	8/6/96	ENV91075.1 (GH-C 3033)	
162-4	Aerobic Aquatic Soil Metabolism	Aerobic Aquatic Metabolism of Fluroxypyr Methyheptyl Ester	Cleveland	6/24/93	8/6/96	ENV91075 (GH-C 3008)	
163-1	Leaching and Adsorption/Desorption	An Adsorption/Desorption Study of Fluroxypyr	Lehmann Miller Olberding	11/4/88	12/9/91	42137319	Acceptable except for mobility of aged ester per EPA on 10/28/92.

Guideline Number	Guideline Title	Study Title	Author	: Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Environn	nental FateTGAI (Co	nt.)					
163-1	Leaching and Adsorption/Desorption	Adsorption/Desorption Batch Equilibrium Partitioning of Methoxypyridine and Dichloropyridinol Metabolites of Fluroxypyr	Cleveland	2/29/96	8/6/96	ENV95072 (GH-C 3854)	
164-1	Soil Field Dissipation Study	Terrestrial Field Dissipation of Fluroxypyr	Poletika	3/21/96	8/6/96	ENV92023 (GH-C 3950)	
164-1	Soil Field Dissipation Study ( Analytical Method)	Determination of Residues of Fluroxypyr ((4-Amino-3,5-dichloro-6-fluoro-2-oxy Acetic Acid) Pyridine), Methoxypyridine ((4-Amino-3,5-dichloro-6-fluoro-2-methoxy) Pyridine) and 3,5-Dichloropyridinal ((4-Amino-3,5-dichloro-6-fluoro-2-hydroxy) Pyridine) in Soil by Capillary Gas Chromatography Using Mass Selective Detection	Moore	8/2/96	8/6/96	GH-C 4170	
See 171-4(e)	Storage Stability (Soil)	(See Residue Chemistry) Frozen Storage Stability Study			8/6/96		
165-1	Confined Rotational Crop Study	(See Residue Chemistry)			12/9/91	42137320	
165-1	Confined Rotational Crop Study	(See Residue Chemistry)			8/6/96		
165-4	Accumulation in Fish	Fluroxypyr Methylheptyl Ester: Letter Report Summarizing Method Development Work for Fish Accumulation Study	Murphy Barron	1/27/89	12/9/91	42137321	
165-4 and 72-6	Accumulation in Fish and Aquatic Organism Accumulation Study	The Bioconcentration and Metabolism of Fluroxypyr 1-Methylheptyl Ester by the Rainbow Trout, Oncorhynchus mykiss Walbaum	Woodburn	6/13/96	8/6/96	DECO-ES-2679	
N/A	Environmental Assessment/Summary for Fluroxypyr	Environmental Assessment/Summary for Fluroxypyr	Cleveland	7/2/96	8/6/96	GH-C 4034	

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Residue (	ChemistryTGAI						
165-1	Confined Rotational Crop Study	14C Fluroxypyr MHE: Confined Accumulation Study on Rotational Crops Planted at 30, 120 and 366 Days After Soil Treatment	Lickly Lardie Miller Baldwin	9/17/90	12/9/91	42137320	Supplemental study (upgradeable) per EPA on 10/28/92
165-1	Confined Rotational Crop Study	A Confined Rotational Crop Study with 14C- Fluroxypyr Methlheptyl Ester	Yackovich	5/8/96	8/6/96	MET92057 (GH-C 3988)	
171-4(a)	Nature of Residue in Plants	Metabolism of [14C] Fluroxypyr MHE in Wheat	Puvanesarajah	10/25/91	12/9/91	42137344	
171-4(b)	Nature of Residue in Livestock	The Fate of 14C Labeled Fluroxypyr Fed to Laying Hens	Yachovich Lardie Miller	1/20/89	12/9/91	42137345	
171-4(b)	Nature of Residue in Livestock	The Fate of 14C Labeled Fluroxypyr Fed to Lactating Goats	Yachovich Lardie Miller	2/12/90	12/9/91	42137346	
171-4(b)	Nature of Residue in Livestock	Nature of Residues of [14C] Fluroxypyr in Lactating Goats	Huskin	5/29/96	8/6/96	RES95025 (GH-C 3954)	
171-4(c)	Residue Analytical Method (Plants)	Determination of Residues of Fluroxypyr in Corn Forage, Grain and Fodder by Gas Chromatography/Mas Spectrometry	VanDyke	11/22/91	Ì 2/9/91	42164503	
171-4(c)	Residue Analytical Method (Plants)	Method Validation for the Determination of Residues for Fluroxypyr in Corn Forage, Grain and Fodder by Gas Chromatography/Mass Spectrometry	Duebelbeis	3/4/91	12/9/91	42164504	
171-4(c)	Residue Analytical Method (Plants)	Fluroxypyr Analysis Using FDA/USDA Multiresidue Methodology	Henley	7/7/89	12/9/91	42137347	
171-4(c)	Residue Analytical Method (Plants)	Validation Report for the Determination of Residues of Fluroxypyr and Fluroxypyr 1- Methylheptyl Ester as the Acid Equivalent in Grain, Straw and Hay of Wheat, Barley and Oats by Capillary Gas Chromatography with Mass Selective Detection.	Olberding	6/4/96	8/6/96	RES95118 (GH-C 4049)	

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Residue (	ChemistryTGAI (Con	nt.)		****			
171-4(c)	Residue Analytical Method (Plants)	Independent Laboratory Validation of Method GRM 96.02 - Determination of Residues of Fluroxypyr and Fluroxypyr 1-Methylheptyl Ester as the Acid Equivalent in the Grain, Forage, Straw, and Hay of Wheat, Barley, and Oats by Capillary Gas Chromatography with Mass Selective Detection	McKellar	8/2/96	8/6/96	RES96044 · (GH-C 4166)	
171-4(d)	Residue Analytical Method (Animals)	Determination of Fluroxypyr Residues in Peritoneal and Subcutaneous Fat	Day	3/3/88	12/9/91	42137349	
171-4(d)	Residue Analytical Method (Animals)	Determination of Fluroxypyr in Milk	Day	3/8/88	12/9/91	42137350	
171-4(d)	Residue Analytical Method (Animals)	Determination of Fluroxypyr Residues in Kidney, Liver and Muscle	Day	3/3/88	12/9/91	42137351	
171-4(d)	Residue Analytical Method (Animals)	Determination of Fluroxypyr in Eggs, Chicken Muscle, Liver and Fat by Gas Chromatography	Woods Yeakle Hutchison Webster	4/2/90	12/9/91	42164505	
171-4(d)	Residue Analytical Method (Animals)	Determination of Fluroxypyr in Eggs, Chicken Muscle, Liver and Fat by Gas Chromatography	Phillips	10/28/91	12/9/91	42164506	
171-4(d)	Residue Analytical Method (Animals)	Validation Report for the Determination of Residues of Fluroxypyr in Ruminant Tissues and Milk by Capillary Gas Ghromatography with Mass Selective Detection	Olberding	6/10/96	8/6/96	RES95164 (GH-C 4048)	
171-4(e)	Storage Stability	Stability of Fluroxypyr in Corn Forage, Grain and Fodder and Wheat Grain and Straw Stored Frozen	VanDyke	8/14/90	12/9/91	42137352	
171-4(e)	Storage Stability	Frozen Storage Stability Study of Fluroxypyr 1- Methylheptyl Ester, Fluroxypyr, 4-amino-3,5- dichloro-6-fluoro-Pyridinol and 4-amino-3,5- dichloro-6-fluoro-Methoxypyridine in Soil	Phillips, A.M.	5/29/96	8/6/96	RES93010/ RES93051 (GH-C 4032)	
171-4(j)	Magnitude of the Residue in Meat/MilkDairy Cows	DOWCO 433 (Fluroxypyr) Residues in Milk and Tissues of Dairy Cows	Roberts Cameron MacDonald Brown	3/27/86	5/21/87	40244338	

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number	Comments
Residue (	ChemistryTGAI (Con	t.)					 
171-4(j)	Magnitude of Residue - Poultry	Determination of Fluroxypyr in Eggs, Muscle, Liver and Fat Tissues from Chickens Administered Fluroxypyr Herbicide	Woods	4/24/90	12/9/91	42137348	
171-4(k)	Crop Field Trials	Determination of Residues of Fluroxypyr in Wheat, Barley and Oat Grain and Straw	VanDyke	11/12/90	12/9/91	42137353	
171-4(k)	Crop Field Trials	Determination of Residues of Fluroxypyr in Wheat Grain and Straw - A Bridging Study	VanDyke	12/6/91	12/9/91	42137354	
171-4(k)	Crop Field Trials	The Magnitude of Residue of Fluroxypyr in Wheat Following Postemergence Application of XRM-5316	Roberts	7/10/96 Amended 7/24/96	8/6/96	RES95051 (GH-C 4063)	
171-4(k)	Crop Field Trials	The Magnitude of Residue of Fluroxypyr in Barley Following Postemergence Application of XRM-5316	Roberts	7/12/96 Amended 7/24/96	8/6/96	RES95051.01 (GH-C 4064)	
171-4(k)	Crop Field Trials	The Magnitude of Residue of Fluroxypyr in Oats Following Postemergence Application of XRM-5316	Roberts	7/10/96 Amended 7/24/96	8/6/96	RES95051.02 (GH-C 4065)	
171-4(1)	Magnitude of the Residue in Processed Food/Feed	Determination of Residues of Fluroxypyr in Processed Fractions of Wheat	VanDyke	9/20/91	12/9/91	42137355	
171-4(1)	Magnitude of the Residue in Processed Food/Feed	Determination of Residues of Fluroxypyr in Wheat Processed Fractions	Phillips, A.M.	1/27/95 and Amended 5/23/96	8/6/96	RES93032 (GH-C 3477)	
171-5, 171-6, 171-7	PESTICIDE PETITION Section E: Reduction of Residue, Section F: Proposed Tolerance, Section G: Reasonable Grounds in Support of the Petition (Acid)	Fluroxypyr in or on Barley, Oats and Wheat: Sections E, F and G of the Petition for Permanent Tolerances	Hamburg	7/30/96	8/6/96	GH-C 4159	
N/A	Residue Chemistry Summary	Interpretive Summary of Fluroxypyr and Fluroxypyr 1-Methylheptyl Ester Residue Chemistry	Olberding	8/2/96	8/6/96	GH-C 4158	

(Data submitted 8/6/96 are listed in BOLD)

Guideline Number	Guideline Title	Study Title	Author	Study Date	Submission Date	MRID Number or DowElanco Study ID Number		Comments
Produci	Chemistry (End-U.	se)Starane* ECprev. XR	M-5316	·			·	
61	Product Identification and Disclosure of Ingredients	Series 61: Product Identity and Composition of STARANE* EC Herbicide, An Emulsifiable Concentrate Formulation of Fluroxypyr-1-Methylheptyl Ester	Paterson	7/8/96	8/6/96	GH-C 4061		
62	Analytical and Certification of Limits	Series 62: Analysis and Certification of Product Ingredients of the End-Use Product XRM-5316, and Emulsifiable Concentrate Containing Fluroxypyr-1-methylheptyl Ester (1-MHE)	Ghaoui	7/17/96	8/6/96	GH-C 4033		

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Series 63: Determination of Physical and

Emulsifiable Concentrate Containing Fluroxypyr

Chemical Properties of XRM-5316, an

1-Methylcheptly Ester (1-MHE)

Physical and Chemical

Characteristics

63

(Data submitted 8/6/96 are listed in BOLD)

Guideline Number	Guideline Title	Study Title	Author Study Date	Submission MRID Number or DowElanco Study ID Comments Date Number
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#### Mammalian Toxicology (End-Use)---Starane\* EC---prev. XRM-5316

	Auminiation Toxicology (End Coo) Sourante Ec provincial Colo								
81-1	l Acute Oral Toxicity in the Rat	XRM-5316: Acute Oral Toxicity Study in Fischer 344 Rats	Cosse	11/20/92	8/6/96	M-005316-001A			
81-2	Acute Dermal Toxicity	XAM-5316: Acute Dermal Toxicity Study in NewZealand White Rabbits	Cosse	11/20/92	8/6/96	M-005316-001D			
81-3	Acute Inhalation Toxicity in the Rat	XRM-5316: Acute Inhalation Toxicity Study With Fischer 344 Rats	Beekman	2/18/93	8/6/96	M-005316-002			
81-4	Primary Eye Irritation in the Rabbit	XRM-5316: Primary Eye Irritation Study in New Zealand White Rabbits	Cosse	11/20/92	8/6/96	M-005316-001C			
81-5	Primary Dermal Irritation	XRM-5316: Primary Dermal Irritation Study in New Zealand White Rabbits	Cosse	11/20/92	8/6/96	M-005316-001B			
81-6	Dermal Sensitization	XRM-5316: Dermal Sensitization Potential in the Hartley Albino Guinea Pig	Cosse	11/20/92	8/6/96	M-005316-001E			



#### UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

#### WASHINGTON, D.C. 20460

August 9, 1996

DOWELANCO
 9330 ZIONSVILLE ROAD
 INDIANAPOLIS, IN 46268

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

ATTN: ROBERT F BISCHOFF

PRODUCT NAME: STARANE F COMPANY NAME: DOWELANCO

OPP IDENTIFICATION NUMBER: 243062 EPA FILE SYMBOL: 62719-EIL EPA RECEIPT DATE: 08/08/96

SUBJECT: RECEIPT OF APPLICATION FOR A NEW REGISTRATION

DEAR REGISTRANT

The Office of Pesticide Programs has received your application for a new registration, and it has passed an administrative screen for completeness.

Please note that this is only a notification of receipt of your application. This is only the first step in the application process, and does NOT constitute approval.

If you have any questions, please contact Joanne Miller, Product Manager 23 at (703) 305-6224.

Sincerely,

Front End Processing Staff Information Services Branch

Program Management and Support Division

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